BRAIN.

PART III., 1906.

Original Articles and Clinical Cases.

ON SOME OF THE NERVOUS COMPLICATIONS OF THE SPECIFIC FEVERS.

BY SIR THOMAS BARLOW, BT., K.C.V.O., M.D.

Presidential Address delivered before the Neurological Society of the United Kingdom on November 1, 1906.

FROM its very inception the Neurological Society has claimed the allegiance and the service of workers in every department of the vast growing body of knowledge with which it is concerned. Thus it has come to pass that physiology and anatomy, the investigation of morbid structure, embryological studies, experimental pathology, psychological speculation, practical experience of insanity, and many other branches of inquiry, have brought valuable contributions to the common store. It seemed to you fitting that, once in a way, a representative of general clinical medicine should have a share in guiding the deliberations of the Society, and in accordance with that decision I have thought that, by way of presidential address, I might offer a few reflections on a pre-eminently clinical subject, viz., on some of the complications having reference to the nervous system which are to be observed in some of the specific fevers.

Consider for one moment the rich harvest of symptoms on the nervous side which are ready for investigation in this group of diseases. The rigor or initial convulsion,

the severe aches and pains in head, eyes, back and limbs, the early vomiting, the early lethargy, the delayed cerebration exemplified by failure in memory and power of expression; then the symptoms of advance:—the delirium replacing the headache, the insomnia and deafness, the tremors of lips, tongue and limbs, the muscular weakness of eyelids and face, limbs and back, the weakened innervation of bladder: then the late and more specialised troubles:—the paresis of ocular muscles and accommodation, the faulty deglutition, the convulsions, limited or bilateral; the hemiplegias and speech defects, the ear troubles and insidious inflammatory deposits with their secondary infections attacking the meninges and elsewhere: the head retraction and opisthotonos, the various forms of ascending paralysis: the post febrile paralyses and atrophies, the psychoses.

The most cursory review convinces us that not only in the sequelæ, nor even in the complications, but in the essential symptomatology of the specific fevers the nervous perturbations loom large, and compel our attention.

In the presence of such a wealth of subjects I have been careful to guard the title of my address with many qualifying adjectives.

The charming papers of Gubler [1], which appeared in the sixties, first opened up the study of this group of ailments in a broad, though somewhat vague and elusive, way. Gubler insisted on the importance of classifying the nervous symptoms associated with fevers according to the period of the fever, *i.e.*, in the period of invasion, advance or decline, in which they severally appeared. Since his time a mass of literature has been accumulated, first in France and Germany, and in later years in England and America. This has been more clinical than pathological, and therefore the speculations to which the subject has given rise have often received but scanty verification. It would be an enormous task to attempt to summarise this literature, or even to indicate all the categories of nervous disorders occurring in or after the fevers. One category, that of multiple neuritis, though only differentiated for a few years,

has threatened of late, like Aaron's rod, to swallow up all the rest. But on that subject I have little to say. I wish specially to deal with what I take to be affections of the cerebrospinal axis.

A general survey shows that although certain diseases have nervous complications and sequelæ, which are characteristic, yet that there is a great deal in common between many examples of nervous disorder which arise in connection with different initial diseases, and the reflection is forced upon us that pathological processes started by distinct specific poisons may produce clinical syndromes, which recur with striking similarity. One of the most clearly-defined groups is diphtheritic paralysis. We recognise this type pretty definitely as to its clinical manifestations: loss of knee-jerks, varying anæsthesia and ataxy, weakness of trunk and limb muscles, paralysis of soft palate, of accommodation, and of ocular muscles, paralysis of vagus, intercostals or phrenic. With respect to its pathology, besides extensive peripheral neuritis, we know that there is some degeneration of the multipolar cells in the anterior cornua, and it is probable that further investigations will verify the contention that there are changes in the nuclei of origin of some of the cranial nerves. Thanks to the researches of Roux, Yersin and Martin [2], we may take it that the nerve degeneration is brought about by the diphtheria bacilli growing in the membrane and elaborating a ferment; that this ferment by digesting the body proteids, forms albumoses, and an organic acid which are poisons to the nerve fibres. The usual delay in what may be called the elaboration of the poison is well known, though it must be remembered that the disappearance of the knee-jerks can be ascertained much earlier than the paralytic signs, and this may fairly be regarded as the initial indication of nerve poisoning, as indeed in some cases it is the only one recognisable. There is some reason to suspect that in proportion to the quantity of poison made is the extent of nerve damage. Martin's researches show the interesting fact that in proportion to the quantity injected into animals will be the rapidity with which the nerve

symptoms appear. Now, in support of the general statement with which I started, it is to be noted that definite cases have been recorded by good observers in which symptoms of paralysis of soft palate, nasal speech, regurgitation of fluids through the nose, paralytic cough associated with weakness of limbs and neck muscles, have occurred in the course of measles [Bergeron (3)], small-pox [Gubler (1)], and typhoid [Nothnagel (4)].

Let it be borne in mind that there is always the possibility of a concurrent or supervening insidious diphtheria in such cases. In the Paris Hôpital des Enfants Assistés, I remember well years ago that it was quite common for diphtheria to supervene on measles, and Dr. West was greatly struck with this sequence amongst the London poor when he first wrote his lectures on Children's Diseases. I have seen in a family epidemic two children die of diphtheria, a third attacked with the same disease and within a few days also develop typhoid. This family was supplied with milk from a dairy which was proved to be insanitary, and it was found subsequently that a considerable number of cases of both typhoid and diphtheria occurred in patients who obtained their milk from the said dairy. It was the undoubted source of a small typhoid epidemic.

Even bearing in mind such possibilities as I have indicated, we may ask whether other acute specific fevers may not give rise to the diphtheria-like paralytic affection, due to similar localisation of lesion in the nervous system, although the poison may be different. But more striking and indubitable examples of similarity in symptoms of nervous disorder supervening on distinct initial nervous diseases can be obtained in the group to which the clinical title of acute general ataxy was given by von Leyden [5], though the more severe and fatal cases are better designated as acute ascending paralysis. The pathological findings seem, as far as they are forthcoming, to justify Westphal's title of disseminated myelitis or, to be more accurate still, disseminated encephalo-myelitis. This group is, I think, the most fruitful in clinical suggestion of all the cate-

gories of nervous complications of the specific fevers. I propose to review briefly some of our knowledge on the subject, even at the risk of telling a twice-told tale, and because it serves as a focus convenient for my purpose, I make no apology for recapitulating the salient features of an old case of my own [6], for the histology of which I had the great advantage of Dr. Penrose's help. The case was that of a policeman, aged 23, who came under my care for measles. I believe it to be best to recount the *post-mortem* findings first, and to take the clinical features afterwards. The rigor mortis was well marked, and the mottled staining of the skin was undoubtedly the vestige of the measles rash. There was consolidation of the lower lobe of the left lung. The trachea and the bronchi showed intense congestion with ecchymoses. The spleen was enlarged and soft, the liver showed some white patches of recent degeneration and one calcareous nodule of uncertain origin. The heart, kidneys and intestines were natural. No tubercular or syphilitic lesions were to be found in the body. The meninges of the brain showed venous distension, but there was no lymph. The gray matter of the convolutions was darker and the brain substance generally softer than natural. There was no gross lesion to be seen in the brain. In the spinal canal there was much venous engorgement outside the theca; no lymph could be seen on splitting up the membranes. The whole cord was swollen and softened, most markedly so in the dorsal region. Opposite the fifth dorsal vertebra it was quite diffluent. The lumbar enlargement, although it felt firmer externally than the rest, showed some softening on section in the lateral and posterior columns, but the grey cornua seemed to have been the seat of small hæmorrhages; they were brownish-chocolate in colour and in some places showed a tunnelled appearance, as though the hæmorrhages had slightly broken down the structure of the cord. The cord and medulla were hardened in a 2 per cent. solution of bichromate of ammonium and were examined by Dr. Penrose. He found the changes to be entirely vascular and universally distributed, but of varying intensity.

There was great engorgement of the vessels. Many vessels were surrounded by a zone of coagulated exudation, and beyond this the surrounding tissue was infiltrated with leucocytes, giving the appearance on transverse section of a series of concentric rings. Besides the extensive diapedesis there was evidence of rupture of vessels and slight interstitial hæmorrhage. The upper dorsal region had suffered most, and this was so soft that sections could not be made. From this region the damage extended upwards to the medulla and downwards to the lower part of the lumbar region. The anterior cornua had suffered most throughout the cord, and it was chiefly in them that the hæmorrhages were found. There was also much vascular engorgement in the anterior and posterior nerve roots. No changes were found in the nerve cells, fibres and supporting tissue of the cord, and staining by Gram's and the ordinary methods failed to demonstrate the existence of micro-organisms. In the medulla oblongata the vascular changes were of the same character as those of the cord, but much less in degree, and there were no hæmorrhages. The changes were most marked in the hypoglossal and vagus nuclei, and greater on the left side than on the right.

This man was admitted to hospital on the second day of his rash. The rash was profuse and the lymphatic glands enlarged, but, although he coughed and was hoarse, there was no audible rhonchus, and the highest temperature for three days was 100·8°. Thus at first the case could not be considered a severe one. He complained much of pain down the sternum and at the epigastrium, which in the light of subsequent events may perhaps have been a girdle pain associated with the early incidence of the myelitis in the dorsal region. On the evening of the third day after the appearance of the rash his temperature rose to 103·8° and he had retention of urine. The urine removed by catheter was clear and free from albumin. On the fourth day he was very drowsy, but could be induced to answer questions in an irritable way. Swallowing was natural, but he required to be persuaded to take food. There was no head

retraction and no stiffness about the back muscles, nor had there been any vomiting or complaint of headache. The pupils were equal, of medium size and reacted somewhat sluggishly to light. There was no ocular or facial palsy, and on this day the tongue was protruded in the middle line. The grasp of the two hands was decidedly weak. Voluntary power over the lower limbs was lost. There was no spasm or pain evoked when the limbs were forcibly moved, but one leg which was semi-flexed by the house-physician was found in the same position some hours afterwards. A pinch was felt and localised by the patient on the two legs, but neither plantar reflex nor knee-jerks could be obtained. There was no ankle-clonus. The retention continued. There was some impairment of the percussion note at the base of the left lung behind and a soft apical systolic murmur was heard. The temperature in the morning was 103·2° and in the evening 104·2°. He was treated with ice-bags to the head and spine, and had one dose of antipyrin of 30 grains, after which his temperature subsided and in a few hours came down to 99°; he became less drowsy and answered questions slowly and intelligently, but otherwise there was no improvement. On the fifth day after the onset of the rash he was less drowsy, he understood and answered questions, but only in a whisper. His cough was muffled and ineffectual. It is clear that there was imperfect closure of the glottis preliminary to the cough. When questioned, he still complained of bad pain down the breast-bone and at the epigastrium, and said there was a heavy weight on it. Besides the paralysis of the lower limbs, absence of reflexes and retention of urine, the weakness in grasp had now increased, and it became clear that the intercostals were paralysed, the upper part of the chest being immovable and the respiration carried on by the diaphragm. The tongue when protruded now deviated slightly to the left. The temperature ranged between 100·2° and 100·8°, the pulse was only 76. During the day the patient became cyanosed, with rapid respiration and tracheal râles, and died at night on the eleventh day of his illness and the fifth day after the appearance of his rash.

I need not labour the points of correspondence between the clinical history and the pathological findings. The important features are the very early appearance of spinal complications and the limitation of the lesions, the vascular changes leaving the nerve elements so far as one can estimate practically intact. We know that measles is a disease which quickly elaborates a soil for secondary infection, but this condition seems too early for a secondary infection, and if it be suggested on the lines of Martin's researches on diphtheritic toxæmia that the lesions are the outcome of toxic products, elaborated ultimately by the measles microbes, one can only emphasise the apparent soundness of the nerve elements which seems to militate against that explanation. There is a marked similarity of spinal lesions and skin eruptions, and likewise of local congestions and ecchymoses of the tracheal and bronchial mucous membranes, which may often be seen in an early fatal case of measles.

One is tempted to ask whether the simplest solution of all, in this case, is that the spinal lesion, the rash and the tracheal and bronchial ecchymoses, were the concomitant results of the same process. When the natural history of the measles microbe has been discovered the true position of these lesions in the cycle of events will, doubtless, be established.

A few years after I had seen the above case I had the opportunity of seeing another of fatal ascending paralysis in the exanthem stage of measles. The patient was a young man in whom the very same *rôle* of symptoms appeared on successive days, which, so far as I could make out, were identical with those of the case just recorded. Also Dr. Newton Pitt [7] has recently recorded a very similar case of acute ascending paralysis in a boy, aged 12, beginning with drowsiness and retention, and fatal on the sixth day from the onset of the measles rash. In neither of these two cases, unfortunately, could an autopsy be obtained.

I think, with a judicious use of the pathological imagination, it would be easy to forecast some of the clinical

varieties of nerve disorders, which might be expected to be produced by varying intensity and distribution of the processes here indicated.

First, let us suppose that during the same early period of the illness there occurred similar lesions as to distribution, but less in amount. It is conceivable that, with an alarming onset of what might be called generalised paralysis if the individual vascular changes were very slight, there might ensue complete recovery. With very little more involvement of the nuclei of the cranial nerves than in our case there might easily have developed defective articulation, phonation and deglutition with paresis of palate, some oculo-motor palsies and some altered innervation of the tongue. It would not be difficult to realise that such a case would, in many respects, simulate diphtheritic paralysis. With similar vascular foci in the cerebellum we might look for some forms of ataxy and for nystagmus.

No doubt the paralysis of the intercostals in our patient, due to the hæmorrhagic softening being at its maximum in the dorsal cord, was one of the gravest features of the case. But let us recall that on transverse section the grey cornua showed vascular engorgement more marked throughout than in any other column. Now, let us suppose that the stress of the storm had been more severe in the lumbar region than was actually the case, and that the anterior horns had suffered in still greater excess than was the case. We should then have obtained a condition of things very like anterior poliomyelitis. Finally, if the involvement of the dorsal region of the cord had not been so profound, it seems not impossible that our patient might have partially recovered, and it is conceivable that his disseminated lesions might ultimately have led to a cicatricial condition, presenting a *simulacrum* of multiple sclerosis.

Let us now inquire whether clinical experience supplies any cases conforming with what I have suggested as possible variations from the one which we have taken as a type. First as to cases milder in degree in which complete recovery occurred. Of these there are several. There is a notable one recorded by James Lucas [8] as far back as

1790, in which paralysis of the lower limbs started on the *sixth* day and retention of urine on the *seventh* day after the onset of the rash of measles. The paraplegia completely disappeared in eight days and the retention in ten days. The patient, who was a woman, had suffered similarly when she had small-pox nine years previously, and had completely recovered. M. Liégard [9] records a case of a child, aged 2, who developed, at the end of a week from the onset of measles, rapidly-increasing weakness of both upper and lower limbs, and of the trunk and neck muscles, along with great difficulty of deglutition and mastication. There was general anæsthesia, but no convulsion, contracture or tremor, and the sphincters acted naturally. The child completely recovered in three weeks.

Some years ago I saw a little girl who, within less than a week from the onset of her rash, developed great weakness of all four limbs, back and neck, and ocular palsy on both sides. She made a complete recovery within three weeks. Dr. Newton Pitt [7] quotes four cases of oculo-motor palsy associated with measles, and one of these (Simonin's case) is very relevant. It started on the third day and cleared up in twenty days. According to the fashionable theory, Simonin refers this palsy to neuritis. I believe the more probable explanation is that it was due to vascular nuclear lesions. There are several cases in children, in which the onset was marked by severe coma and prolonged unconsciousness. Batten [10] records one in which, after vomiting, unconsciousness and general convulsions, there remained, slow, hesitating speech, inability to sit up, and some incoördination in upper and lower limbs. The ataxy improved a little in hospital, but very slowly. At a later period it was found that the boy's moral sense was much perverted. Batten, as I believe, quite justly designates this as a case of encephalitis of the cerebellum.

In Colcott Fox's [11] case, along with weakness and ataxy of upper and lower limbs, and slow, difficult articulation, there was occasional nystagmus and much nodding and rolling of the head. There was slow improvement and almost complete recovery within seven months.

I have not referred to cases of hemiplegia. There are many examples following measles. I will discuss this subject subsequently, but I believe it will be found generally, that in the group of disorders now under consideration, which for the most part appear early within the exanthem period, or soon after it, the Rolandic area, and the great basal ganglia are seldom separately affected.

Dawson Williams [12] has recorded a case with extreme care and detail of a girl, aged 3 years and 8 months, who during the exanthem stage of measles was seized with convulsions. She was unconscious for ten days, and on the recovery of her senses could not speak or use her limbs properly. There was some difficulty in swallowing the food, which required to be pushed to the back of the tongue. There was paresis of all four limbs and partial anæsthesia of the lower limbs. By degrees sensation returned. In six weeks there was considerable improvement. She was able to walk and talk a little, using single words, but she showed much incoördination in carrying the food to her mouth and definite intention tremors became manifest. Her speech further improved, but was for years syllabic in character, and even after six years old it remained very deliberate. The knee-jerks were exaggerated and her gait was for a time, somewhat spastic, but it so far improved that when she was ten years old she could walk as far as six miles, rapidly and steadily with short steps, but she was easily upset. She was backward at school, but her mental deficiency was not so great as her vacant expression would suggest.

The resemblance of this case to one of disseminated sclerosis is on the first blush very striking, and it seems probable that some permanent cicatricial changes had supervened upon the earlier vascular disturbances allied to those of our initial case. But the disorder did not progress from bad to worse as a typical disseminated sclerosis case would ultimately have done. Dawson Williams emphasises that there was progressive improvement up to a certain level.

With respect to anterior poliomyelitis, I may refer to

a case which was partly under my care at the London Hospital, but the pathology of which was investigated by F. Charlewood Turner [13] and recorded by him in the "Pathological Transactions" for 1879. It was that of a child aged 2½ years admitted a fortnight after the onset of the paralysis. The lower limbs were definitely paralysed, the upper slightly so, and when admitted there was head retraction. The child began to improve in hospital, the head retraction passed off, free movements of the arms became re-established, and the legs, which had been absolutely immobile, began to respond slightly to tickling of the soles and the toes were moved. Then the child contracted measles. There was undoubted recrudescence and increase of the paralysis of the limbs, and the child died on the eighth day from the onset with much dyspnœa and suppression of urine, although the temperature had subsided on the sixth day.

On *post-mortem* examination, disseminated patches of broncho-pneumonia were found. On section of the spinal cord, the gray matter was seen to be pink throughout. There was hæmorrhagic softening with a ragged cavity, resulting from the breaking down of tissue in the left anterior cornu in the lumbar enlargement. Both anterior cornua throughout the cord showed great vascular involvement with concentric sheaths of corpuscles round the vessels. There was much leucocytic infiltration beyond, and considerable destruction of polar cells and nerve fibres. But the posterior grey cornua also showed vascular changes, though of less degree. There were likewise changes in the white matter, most noticeable in the antero-lateral columns, consisting of enlargement and apparent increase in number of the connective tissue corpuscles, and in wasting of axis-cylinders of nerve fibres and disappearance of their sheaths. I have no doubt that some of these vascular changes were induced by the supervention of measles. In this connection, Charlewood Turner refers to one of Roger and Damaschino's [14] cases of early infantile paralysis in which autopsy was obtained.

The child was admitted with recent paralysis and atrophy of the left deltoid, and slight weakness of the left leg.

The child contracted in hospital an exanthem, which was ultimately considered scarlet fever. During the prodromal stage, which lasted one week, when measles was suspected, *both the legs became paralysed*. At the autopsy the spinal cord showed characteristic softening and leucocytic infiltration, atrophy of ganglion cells, and a general localisation of lesion corresponding in the cervical and lumbar regions with the paralysed limbs.

Now, it may be held that the generalisation of the lesions in our initial case is strongly opposed to any comparison whatever between disseminated myelitis and acute anterior poliomyelitis. On this subject I would like to make some comments. I have long been convinced that anterior poliomyelitis is not necessarily the localised malady which systematic teaching has in the past tended to make it. I believe the sound position to take is, that as there are all grades of motor damage, so the storm of which the centre is in the anterior cornua may involve the other columns in varying degree. The initial febrile stage would seem to suggest a widespread vascular storm, which ultimately spends itself in the anterior cornua where there is anatomically a richer supply of vessels ready to undergo morbid changes than any other part of the cord.

Let us consider three of the pathognomonic signs which are constantly given, namely, (*a*) that there is no sensory alteration in the disease; (*b*) that the sphincters always escape, and (*c*) that the extent of permanent damage is definitively laid down in the early stage, and that further mischief does not occur. Sensory alteration is not easy to test in young children. But in severe cases during the early stage there may be no reflex withdrawal of the leg when the soles are irritated, and no expression of pain. The non-withdrawal of the leg might be due to motor weakness, but the absence of expression of pain could not be so explained. In the other direction that is manifestations of pain, there sometimes occur symptoms which have not received adequate attention, namely, pain and tenderness down the back, stiffness of the back, and hard retraction. These may be due to concomitant meningeal

vascularity and irritation, or to some involvement of the posterior roots. Again, there is sometimes localised exquisite tenderness along the track of one or more nerve trunks associated with localised puffiness, heat, and shiny redness about the lower extremities, very suggestive indeed of concomitant neuritis.

With regard to the sphincters, again, it is not easy to test the real state of things in young children. But it is significant that for some days in the early period the child may pass its evacuations under it. In the London Hospital case, that I have briefly narrated, the child was admitted fourteen days after the onset of the paralysis, and she was in hospital eighteen days before the onset of the measles. During all that time she passed her evacuations involuntarily.

Some years ago I had under my observation a girl, aged about 11 years, who had extensive typical infantile paralysis with characteristic history dating from an early period of childhood. She had an absolutely flaccid anus, and had suffered from incontinence of fæces from the time of her initial illness.

I recall the case of an adult who presents now the typical signs of a severe arrested acute anterior poliomyelitis, with groups of atrophied muscles picked out in a characteristic way in both lower limbs. During the early stage of his illness, when I first saw him, he suffered from retention of urine lasting for several weeks and requiring the use of a catheter. He recovered entirely as far as that function was concerned. As to the definitive character of the process in poliomyelitis, although that is perfectly true in the majority of cases, it is very far from being universally so. I have already shown how the supervention of measles and of scarlet fever led to definite increase of the paralysis. But I have seen a few cases in which, after varying intervals and without the intercalation of any known exanthem, a definite and more severe accession of paralysis has supervened. Moreover, there are cases in which anterior poliomyelitis behaves very much like acute ascending myelitis.

Thus a girl, aged 12, developed signs of poliomyelitis in all four limbs. She then became dyspnœic with intercostal paralysis and died. Risien Russell examined the cord and had no doubt as to its being an example of poliomyelitis of moderate severity. With respect to the rare examples of co-existing cerebral paralysis, the only instance which I have seen was one in which one facial nerve became paralysed along with extensive poliomyelitis. In this case there also occurred marked dyspnœa depending as I believed on failure of intercostals. To my great surprise the patient recovered and survived with only paralysis of limbs. There was no indication of hemiplegia or involvement of higher cerebral centres. I believed the temporary facial palsy which lasted under a fortnight was due to a slight nuclear vascular lesion without destruction of nerve cells, and that so far the case presented some resemblance to the disseminated myelitis group, in which as we have seen the medulla, may be involved to a varying degree. Redlich [15] has indeed found lesions in the medulla and pons in a case of poliomyelitis, but there is, so far as I know, no pathological evidence that in a case of poliomyelitis true hemiplegic lesions have occurred. Henoch [16] and James Taylor [17] have each recorded a case of facial palsy in which the facial affection cleared up, although the limb trouble remained.

To sum up, we are still ignorant as to the *materies morbi* of infantile paralysis, and search for a micro-organism as an essential factor in its production has hitherto been fruitless. Meanwhile it is well to remember the varying conditions under which it has arisen. Amongst these there seems no doubt that measles, scarlet fever, typhoid, chicken-pox are to be reckoned with, and that in more or less close association; also that the morbid anatomy shows definite affinities, though not identity, with the disseminated myelitis which we have been considering. It is now time to give evidence of the contention made at the outset of this paper that the group known clinically as acute central ataxy, and pathologically as disseminated encephalo-myelitis, includes examples drawn from distinct specific fevers.

First in importance come the clinical papers of Westphal [18] describing a special affection of the nervous system after small-pox and typhus. The small-pox cases are the most striking. The nervous phenomena may begin very early, even in the prodromal stage, as Trousseau also pointed out. There is first prolonged coma, then speech disturbance—slow, drawling, sometimes even scanning in character, but in any case the separate syllables spaced out and uttered with difficulty. There may be constant difficulty with certain consonants. The voice is high pitched, nasal and without modulation. In some cases there is difficulty of swallowing. Then comes the shaking of the head, at first inability to stand or walk, then ataxy of both upper and lower limbs and intention tremors. Slow improvement.

The symptoms in the typhus case showed much resemblance to those of the small-pox cases, but were first noticed after the patient had been five weeks in bed. Ebstein's case [19], which occurred in connection with typhoid, began with eight days of unconsciousness. It resembled the other cases in regard to the speech alteration and ataxy. There was difficulty in protruding the tongue, and an atropic patch in the middle of the tongue was present. Like the other cases, after a time it came to a standstill. *Post-mortem* examination of this case (fatal not from the nervous disease, but from the supervention of phthisis) showed scattered areas of sclerosis in gray and white matter in the cord, and also in the medulla; and there was definite change in the nucleus of the right hypoglossal. The *post mortem* was made seven years after the onset of the nervous symptoms.

Whipham and Myers [20] have given the most complete clinical report extant of two cases of speech defect and ataxy following on small-pox. Their valuable appendix gives a *résumé* of other cases under the care of German and French observers up to the date of their paper. Of the initial diseases variola is by far the most common, but typhoid, measles, pneumonia, ague and erysipelas, also afford good examples. To these I may add a case of my

own of scarlet fever as well as one of small-pox. There are some differences as to the period of illness, when the first nervous change was observed, and there are inadequate details in some cases, which had only come under the observation of their respective reporters after a considerable interval from the initial illness. As to the progress of the symptoms, it will be found that the cases group themselves roughly into those in which, within a month's time, there is complete recovery, and those which ameliorate up to a certain level, but in which some ataxy of limbs and some articulatory defect is permanent. But the natural history of these cases differs from that of multiple sclerosis in this respect, that when the above symptoms have arrived at a certain level they do not appear to develop further in a downward direction. There is no further dissemination. This, at least, is the conclusion obtained from observation over several years' duration in some of the best recorded cases, and this agrees with Dawson Williams's conclusion already mentioned with respect to his measles case.

Next in order for consideration comes the important paper of Westphal [21], in 1873, on disseminated myelitis, giving the record of two fatal cases which had supervened upon small-pox. The first of these cases shows a remarkable resemblance both clinical and pathological to the measles case with which we started. The chief differences are date of onset and duration. The symptoms of paraplegia, with absolute motor paralysis and partial anæsthesia, began on the eleventh day after the onset of the rash, and the patient died in four weeks. The *post mortem* showed disseminated myelitis of the same character as that already described with absence of any damage to the ganglion cells. The later researches on fatal cases of disseminated myelitis, and of what may be included under the general term of acute ascending paralysis, have been rendered more searching and exhaustive by modern methods of staining. Moreover, in a few cases bacteriological examination has shown the existence of pathogenic organisms in the cord, meninges and cerebrospinal fluid, and sometimes in the blood and other organs of the body.

Farquhar Buzzard [22], in his valuable contribution to the pathology of Landry's paralysis has given a synopsis of these cases. The most important, especially if it receives subsequent verification is Curschmann's identification of typhoid bacilli in the cord of an enteric fever patient who had an ascending myelitis. I have refrained from referring hitherto to Landry's paralysis as such, because provisionally, at all events, the term should not be applied to those cases of ascending paralysis which arise in connection with the true specific fevers, and in which there are gross vascular lesions. But the later researches, which show under new methods of staining increasing evidence of definite change in the cord, of *toxic* character, and of the frequent involvement of the spleen, and thereby the presumption in favour of blood disease, must compel, in the future, the study of this disease in conjunction with our group. The diplococcus found by Risien Russell [23] in a case of acute ascending meningo-myelitis, which was under Dr. Buzzard's care, is of special interest, because it has some points in common with Weichselbaum's diplococcus, and likewise with its ally, the diplococcus found by Still in posterior basic meningitis.

In Sir William Gowers' case of Landry's paralysis, which was investigated by Farquhar Buzzard, a micrococcus was isolated from the blood of the patient, and one indistinguishable from it was found in the external part of the spinal dura mater, although it could not be found in the cord itself. Subdural injection of a cultivated micrococcus into a rabbit produced, after some days, a rapidly-spreading palsy, and this same organism was found in the spinal dura and likewise isolated from the blood. Speaking entirely from the clinical side, I trust it will not be thought obscurantist if I express the hope that further research might show that, not only in Landry's paralysis, but in disseminated myelitis generally, different organisms should be found capable of bringing about a sum total, which, in different diseases, would be practically the same.

The subject of multiple peripheral neuritis, in relation

to the acute specific fevers, is too large to enter upon in this address, but I will venture to submit three brief suggestions for your consideration.

The subject of multiple neuritis in relation to the fevers is much too large to discuss in detail. I will confine myself to three suggestions:—

(1) It would seem that the element of time is an important one generally in the production of polyneuritis, if the view be accepted that the change is of the nature of a segmental degeneration, and that the irritant is a toxine elaborated as the result of the microbic development within the body of the patient. We should, therefore, be inclined generally to look for the appearance of this group of lesions at a later period than those which have formed the principal subject of our consideration to-night. Multiple neuritis in its full expression belongs to the progressive sequelæ rather than to the complications, though its initiation may have an early start as we see in the early loss of knee-jerks in diphtheria.

(2) It would seem from the results of the newer staining methods that the undue anxiety to exclude the cord from any participation in the *rôle* of multiple neuritis was somewhat premature.

One may hope that in time further verifications may be forthcoming of the pregnant suggestion of Sir William Gowers that the initial change may, after all, start in a toxic alteration of the multipolar cells of the anterior horns

(3) The clinical facts brought forward in the Manchester arsenical beer neuritis cases seem to show how arsenic and alcohol, when combined, mutually reinforced one another in producing a result which, for virulence, was greater than either of them might have been expected to produce, even if given in larger amount and over longer periods than was actually the case. By analogy, is it possible that, in some of the cases of prolonged neuritis after typhoid, the effect of the febrile toxines and of moderately large doses of alcohol given every two hours through several weeks may produce in like manner a very tangible combined result.

Now permit me to say a few words about the difficult

subject of hemiplegia in relation to the specific fevers. A large number of the cases of hemiplegia in connection with specific fevers are in children, and it may be convenient at the outset to narrow down the consideration of the subject accordingly. Taking first the main clinical features, it may be stated that the hemiplegias associated with the fevers are generally ushered in by a series of convulsions either unilateral on the side which will subsequently be paralysed or bilateral, or both. There is generally some fever, and there is often absolute speechlessness for a day or two after recovery from the convulsions. Typical aphasia may be present for a few weeks, but in most cases it ultimately clears up. The only two cases of permanent aphasia in children that I have ever seen were both cases of bilateral brain lesions. One proved to be due to embolic softening in the third frontal convolution on both sides, and the other was almost certainly due to syphilitic arterial disease on both sides of the brain in similar situations.

The facial weakness is barely detected when the patient is at rest, and is often more marked by contrast with the sound side under emotional than under volitional stimulus. The arm generally suffers more than the leg, and the spastic condition on the paralysed side sometimes supervenes very early indeed.

So far as I have seen, the earlier in the acute illness the hemiplegia appears the more likely is it to recover completely. All the cases that I have known in connection with pneumonia have completely recovered, but recovery during *delayed convalescence*, as, for example, after scarlet fever when dropsy has been present, is of more serious prognosis, and these post-febrile cases supply us, after a lapse of years, with some of our examples of athetosis and its allies.

As to the pathology of post-febrile hemiplegias, it is no doubt attractive to place these cases alongside those of early disseminated myelitis, and to regard them as due to one-sided localised cortical encephalitis or encephalitis of the neighbourhood of one of the basal ganglia. I have no personal experience of autopsies which support this view.

Moreover, as I have already pointed out, careful study of those cases in which articulatory defects, ataxy, and intention tremors, remain for a longer or shorter time, seems to exclude the definite and localised participation of the Rolandic areas and the basal ganglia, so far, at all events, as clinical signs indicate.

Let me repeat that it would seem to be the back part of the brain along with the hypoglossal, the vagus, and the oculo-motor nuclei, that appears to suffer in a definite and sometimes temporary, sometimes persistent, way. The cortical involvement at the very outset would seem to be transient, general, and not localised.

But although the eruptive fevers have supplied us with very little evidence of hæmorrhagic encephalitis in the fore and middle parts of the brain, there is a certain amount of evidence derived from epidemic influenza. This disease, as is well known, lends itself to mixed infections, and we must exclude cases of purulent meningitis, of which there are a few on record, also the two important cases of cerebral abscess narrated by Bristowe [24].

Senator's case [25], the *post mortem* of which was made by Virchow, was surely an instance of mixed infection, and is of interest as showing combination of purulent and hæmorrhagic lesions.

The patient was a man, aged 33 years, who early in the course of what Senator diagnosed as influenza, developed somnolence, prostration, pyrexia, epistaxis, right hemiplegia. At the autopsy, besides a hæmorrhagic focus as big as a small apple in the left hemisphere, there were some smaller hæmorrhages, two small abscesses, and a little local meningitis. There was also hæmorrhagic nephritis, small abscesses in the liver, and slight mitral endocarditis; but Virchow was unable to decide as to what was the starting point for the different abscesses.

In Fürbringer's first case [26], which occurred at the same time as Senator's, there were found hæmorrhages in the central convolutions on both sides the size of a hen's egg. There was thrombosis in the sinuses, some hæmorrhage in the retina, disseminated broncho-pneumonia, an

enlarged soft spleen, and the mucous membrane of the small bowel was infiltrated with blood.

The patient was a maid-servant, aged 23 years, who suddenly sickened with what was believed to be influenza, and had temporary loss of sensation, and weakness in the right arm. She got about after the first day feeling very weak, and having considerable bronchitis, but the weakness and loss of sensation in the arm passed away. In a few days, whilst up and at work, she became suddenly worse, with headache and recurrence of loss of sensation and power in the right arm, and then weakness of the right side of the body, vomiting, gradual loss of consciousness, and convulsions supervened. She was only under Fürbringer's observation for two days, and her highest temperature was 40·8 C. She was unconscious all the time; there were some signs of irritation such as grating of the teeth, and the extremities were sometimes rigid, sometimes flaccid. The repeated convulsions affected the face and all four extremities, and there was ultimately flaccid paralysis of the limbs, and loss of knee-jerks.

Passing from these fulminating cases, in which there were large focal hæmorrhages, we arrive at some others, in which the lesions found were certainly more allied in character to the disseminated myelitis group.

Thus in Fürbringer's second case on *post-mortem* examination the whole region of the central ganglia was found softer than natural, yellowish in colour, both in spots and diffused, and especially in the white substance, pervaded with punctate and streaky hæmorrhages, but there were no large extravasations. There were minute hæmorrhages also in the crura cerebri, the cerebellar hemispheres, and the pons. The heart was intact, there were large and small areas of consolidation in the lower lobes of both lungs. The spleen was engorged.

This patient was a previously healthy man, aged 32 years, who kept about for five days suffering definite influenza, and feeling on the fifth day much better, partook of a hearty meal. Next day he had a relapse, with nausea, vomiting, and oppression over the stomach. Then succeeded feverish-

ness, retraction of abdomen, and restlessness, marked blunting of the sensorium, and on the eighth day sluggish pupils and stiffness of the neck. The man became unconscious, with incoördination of eye movements and nasal breathing. There was incontinence of urine and fæces. The temperature gradually rose from 36° C. to 40·6° C. The pulse, which was at first only 76, became smaller and more frequent, there was great increase of respiration frequency (up to 56) and signs of œdema of lungs; death occurred on the ninth day from the onset of the influenza.

During the two days that he was in hospital the patient was thought to be suffering from meningitis.

In Koenigsdorf's case [27] on *post-mortem* examination of the brain there was found thrombosis of the transverse sinus, and of one of the larger veins at the base, but the brain arteries were normal. The walls of the lateral ventricles were pervaded with numerous punctiform hæmorrhages. The white substance throughout a large extent was of pale citron yellow colour, and moderately softened. There were also numerous punctiform hæmorrhages, and in the left optic thalamus a focus of red softening. The cortex and the basal part of the brain and the cerebellum were normal. Beyond bronchitis and some collapse, and enlargement and engorgement of the spleen, there was nothing important in the viscera.

Microscopic examination of the left optic thalamus showed extensive infiltration of leucocytes, giving rise in different areas to marked sheathing of the vessels. The capillary apoplectic areas were irregularly circumscribed. Degenerative changes of the nuclei of the round cells were either not present at all, or only to a very slight degree. The supporting tissue of the glia was well defined. Ganglion-cells and nerve-bundles were unchanged. No embolic infarction with bacteria was found, and indeed no evidence whatever of the presence of bacteria could be obtained by Gram's and Löffler's methods.

The patient was a young, previously healthy woman, aged 21 years, who on the third day after the onset of influenza suddenly became unconscious. When admitted

she could not be roused. There was no head retraction; there were slight lateral movements of the eyeballs and the pupils were sluggish to light. The jaws were firmly closed and remained so to the end. There were slow movements of the left upper extremity. The muscles of the extremities were slightly rigid. The patellar reflex was present, and equal on the two sides. The skin reflexes were slight. There was incontinence of fæces and urine. The temperature was 37·7°, and the pulse was full, strong and regular, 60.

During the four days that she was in hospital the right upper extremity became completely limp, the slow movements of the left arm continued more or less; the coma continued, the temperature rose to 39·8°, and the pulse and respiration became more frequent. She died on the eighth day.

James Putnam [28] records a case on which *post-mortem* examination showed that the whole brain was œdematous, and that in the right basal ganglia and internal capsule there was yellow discolouration and slight softening, and, to a less degree, the same conditions in the left internal capsule. Microscopic examination showed capillary and small arterial hæmorrhages, and leucocytic infiltration.

The patient was a lady, aged 71 years, without any indications of cardiac or renal disease. She had a well-marked attack of influenza. She was convalescing, and was well enough to be up and dressed, though she was not strong. She suddenly became unconscious for a quarter of an hour, without other symptoms. Three days later she had twitching of the left side of the face, and afterwards twitching of the left arm. These attacks recurred with increasing severity for three hours, and were succeeded by left hemiplegia and loss of consciousness. There was some recovery of consciousness, but she died next day without further symptoms.

Prickett and Batten [29] report the case of a boy, aged 9 years, who had suffered, along with other members of his family, from a moderate attack of influenza, with some fluctuation. The boy had been allowed to go to a chil-

dren's party, and his cough had become worse. Five days afterwards he woke in the morning with odd sensation in his right arm. The arm was found to be helpless, and when seen shortly afterwards by Dr. Prickett the right arm and leg had become completely paralysed, there was deviation of eyes and head to the left, and the boy was aphasic. His temperature was only just above normal, and his pulse about 90. He became drowsy, cried out occasionally, and put his left arm up to the head as though in pain. He grew rapidly worse, passed into a state of coma, and died three days after the onset of the paralysis.

Post-mortem examination of the brain showed engorgement and thrombosis of the vessels of the subcortical white matter of the frontal parietal and occipital regions, especially on the left side, but to a slight extent on the right side also. There were also small blood extravasations in the neighbourhood of vessels, and independently of vessels. There was round-celled exudation, some of the cells being of the normal size of leucocytes, and others much smaller. These small cells Batten was inclined to regard as blood platelets, and he directs attention to the excess of blood platelets in the blood of infectious diseases, and their possible bearing as a factor in thrombosis. The cells of the cortex, examined by Nissl's method, were swollen and globular, their nucleus and nucleolus normal, but the chromophile substance was finely granular and stained feebly.

No cultures were made from the brain in this case, but Batten quotes two cases of encephalitis in which Pfeiffer's bacillus was found, viz., one by Nauwerck and one by Pfuhl, the latter being, however, one of mixed infection.

In reviewing these and other cases of influenzal encephalitis it is clear that they are by no means limited to young subjects, and that the initial attack is not necessarily a severe one. It is important to note that they occur within a few days of the onset, or in the treacherous early days of convalescence, when the patient moves about or goes to work feeling weak, and when relapse of the disease is so

common. It would also appear that after the initial head pain and vomiting the monoplegia and ill-defined hemiplegias are very rapidly followed by more or less generalised paralysis, and that the convulsions are often bilateral. The duration is very short (three or four days) and although the temperature rises during the last day or two it is not markedly elevated at first. In the imperfect localisation and rapid generalisation of symptoms the cases present much resemblance clinically to purulent meningitis.

Although, as a rule, very fatal, there are several cases on record, recorded by Oppenheim [30] and others which presented the above features in a mild form, and in which recovery took place.

I have laid great stress throughout on the early period of febrile diseases in which certain nervous manifestations occur, but it is time to consider the post-febrile hemiplegias (especially of children) which supervene in the later periods.

Can these be explained by the hypothesis of hæmorrhagic encephalitis? I think the older pathology of embolism and thrombosis is more probable as an explanation of this group. There is at all events some *post-mortem* evidence to show that definite thrombosis in one or more of the larger arteries at the base of the brain and in their branches may occur. Thus in a case of diphtheria in a boy of 7 years old the membrane had cleared from the throat and the albumin had disappeared from the urine at the end of a fortnight, and then after two convulsions the boy got complete left hemiplegia. Ultimately he showed typical naso-pharyngeal paralysis, and died from paralysis of the intercostals. At the *post mortem* Dr. Abercrombie [31] found the right middle cerebral artery occluded at its bifurcation by a firm, pale adherent thrombus.

In a little girl suffering from noma vulvæ, who got unilateral and bilateral convulsions, followed by hemiplegia, I found thrombi of different ages in one middle cerebral and some of its branches, and in the left auricular appendix, partly decolourised laminated clots, some of which were liquefying in the centre. I am tempted to refer to three cases of post-scarlatinal hemiplegia, in which, though there

was no autopsy, I believe the evolution of the symptoms gave a strong presumption in favour of dilatation of the heart, cardiac thrombosis, and cerebral embolism, as the etiological factors.

The first was a little girl, who, at the end of her desquamation, was brought to me with great dyspnœa of the air-hunger type, and some cyanosis, associated with undoubted dilatation of the left side of the heart. No murmur was detectable, but the heart's apex was at least one inch external to the nipple line, and there was marked irregularity with ill-defined first sound. Within three days of her admission there was remarkable improvement under rest, ether, and digitalis, so that, to my surprise, the apex beat had returned almost to the nipple line. There then suddenly occurred a severe convulsion followed by right hemiplegia, and, for a short time, speechlessness. The speech returned and the hemiplegia slowly improved, but did not clear up entirely. I believe this child had a cardiac thrombus, some of which was displaced as the heart recovered in some degree from the toxic dilatation, which is not uncommon as a result of scarlet fever.

A boy was brought to me with right hemiplegia, and I found in the course of examination that he was blind with the left eye, and that he had atrophy of the left disc. The right fundus was natural, and with the right eye his vision was good. From the careful history obtained from his mother I ascertained that he had suffered a few months previously with scarlet fever, followed by dropsy. During the dropsy he became exceedingly breathless, and then passed into a state of unconsciousness. He subsequently developed paralysis of the right side. He recovered from his dropsy and breathlessness, but the paralysis remained. The boy presented no cardiac lesion when he came under my care, but I believe the most reasonable explanation of his symptoms to have been that during the dropsy he suffered from cardiac dilatation and cardiac thrombosis, that some of the cardiac thrombus was carried to his left middle cerebral artery, giving rise to the right hemiplegia, and a small portion was carried on to the central artery

of his left retina, causing the blindness and atrophy of the disc. A valuable series of cases presenting this combination of symptoms has been recorded by Batten and Guthrie [32].

In a third case, a young woman came under my care with the clear history given to me by her mother of scarlet fever some years previously, directly followed by dropsy in which there was a period of breathlessness and subsequent convulsions and consecutive hemiplegia. The hemiplegia improved, but left her with occasional convulsions and athetosis, for which she was brought to hospital.

Thrombosis of cerebral sinuses is, I think, hardly sufficient to explain the post-febrile hemiplegia. It is true that small extravasations in the cortex are sometimes found *post mortem* in considerable amount as an accompaniment and probably result of sinus thrombosis, but they are generally bilateral and extensive, and although they are sometimes responsible for severe screaming attacks and even convulsions, in the patients that I have traced hemiplegia has not been present. I might also refer to the purpura which sometimes complicates the fevers and may be accompanied, especially in typhoid, by extensive blood extravasations into the arachnoid cavity and elsewhere. But the symptoms beyond torpor and coma are too vague to justify useful clinical conclusions and hemiplegia is not one of them.

I have already trespassed too long on your patience, though there are many other branches of this subject which deserve enquiry, and with which I am not competent to deal. The meningeal complications I have refrained even from mentioning because they open up the large subject of secondary infection which ought to be separately considered. But grievously inadequate and incomplete as I am only too conscious these observations have been, they will not have been entirely useless if they serve to emphasise the note with which I started; and you will agree with me, that this subject is one of those which this society is pre-eminently qualified to advance on to a higher plane. It is in subjects like this that the young and skilled and ardent investigators of morbid histology will come with the results of their

labours to stimulate and help clinical workers towards wider knowledge and broader views.

References.

[1] Gubler. *Arch. gen. de Méd.*, 1860, Tom. i., p. 402.
[2] Martin. *Proc. Royal Soc.*, 1892, vol. li., p. 78.
[3] Bergeron. *Gaz. des Hôpitaux*, 1868, p. 5.
[4] Nothnagel. *Deutsch. Archiv. fur Klin. Med.*, 1872, S. 480.
[5] Leyden. *Zeitschrift f. Klin. Med.*, 1891, Band xviii., S. 576; also *Deutsche Med. Woch.*, 1892, Nos. 27 and 28.
[6] Barlow and Penrose. *Med. Chi. Trans.*, 1887, vol. 70, p. 77.
[7] Newton Pitt. *Trans. Clin. Soc.*, 1904, vol. xxxvii., p. 23.
[8] James Lucas. *Lond. Med. Journal*, 1790, p. 325.
[9] Liégard. *Gaz. des Hôpitaux*, 1859, p. 562.
[10] Batten. *Trans. Clin. Soc.*, 1905, vol. xxxviii., p. 193.
[11] Colcott Fox. *Lancet*, 1887, vol. i., p. 771.
[12] Dawson Williams. *Med. Chi. Trans.*, 1894, vol. lxxvii., p. 57.
[13] Charlewood Turner. *Trans. Path. Soc.*, 1879, vol. xxx., p. 202.
[14] Roger and Damaschino. *Gaz. Médicale de Paris*, 1871, pp. 457, 480, 505, 541, 576.
[15] Redlich. *Wien. Klin. Woch.*, 1894, No. 16.
[16] Henoch. 1889, vol. i., p. 256 (*Thomson's Trans.*, 1894, No. 16), *New Sydenham Soc.*
[17] Jas. Taylor. "Nervous Diseases in Childhood," London, 1905, p. 371.
[18] Westphal. *Archiv. für Psychiatrie*, 1872, Band iii., S. 376.
[19] Ebstein. *Deutsch. Archiv. für Klin. Med.*, 1872, Band x., S. 595, and Band ix., S. 595.
[20] Whipham and Myers. *Trans. Clin. Soc.*, 1886, vol. xix., p. 164.
[21] Westphal. *Archiv. für Psychiatrie*, 1874, Band iv., S. 338.
[22] Farquhar Buzzard. *Brain*, 1903, vol. xxvi., p. 94.
[23] Thomas Buzzard and Risien Russell. *Trans. Clin. Soc.*, 1898, vol. xxxi., p. 185.
[24] Bristowe. *Brit. Med. Journ.*, 1891, ii., p. 6.
[25] Senator and Virchow. *Deutsch. Med. Woch.*, 1891, No. 49.
[26] Fürbringer. *Deutsch. Med. Woch.*, 1892, No. 45.
[27] Koenigsdorf. *Deutsch. Med. Woch.*, 1892, No. 9.
[28] James J. Putnam. *Boston Med. and Surg. Journal*, 1892, vol. xxvii., p. 349.
[29] Prickett and Batten. *Trans. Clin. Soc.*, 1900, vol. xxxiii., p. 157.
[30] Oppenheim. *Deutsche Zeitschrift für Nervenheilkunde*, 1895, Band vi., S. 375.
[31] Abercrombie, John. *Trans. Internat. Med. Congress*, 1881, vol. iv., p. 61.
[32] Batten and Guthrie. *Trans. Clin. Soc.*, 1903, vol. xxxvi., p. 52.

THE DEVELOPMENT OF THE VERTEBRATE NERVE-CELL: A CYTOLOGICAL STUDY OF THE NEUROBLAST-NUCLEUS.

BY JOHN CAMERON, M.D., D.Sc., F.R.S.E.,

Senior Demonstrator of Anatomy, University of Manchester.

CONTENTS.

(1) INTRODUCTORY 332
(2) THE ASSIMILATIVE POLE OF THE NEUROBLAST-NUCLEUS 333
(3) THE NASCENT OR EMBRYONIC AND THE MATURE OR ADULT CONDITION OF NERVE-CELL CYTOPLASM 336
(4) CHANGES EXHIBITED BY THE NEUROBLAST-NUCLEI AS EVIDENCE OF THEIR METABOLIC ACTIVITY 346
(5) THE α-, β- AND γ-NEUROBLASTS 348
(6) THE PRESENCE OF NUCLEAR DERIVATIVES IN THE CYTOPLASM OF NERVE-CELLS 351
(7) THE BEHAVIOUR OF THE NEUROBLAST-NUCLEI COMPARED WITH THAT OF THE NUCLEI OF ACTIVELY FUNCTIONING NERVE-CELLS 353
(8) SUMMARY OF RESULTS 356
(9) LITERATURE 358

(1) INTRODUCTORY.

THE development of the central nervous system has for long provided a rich source of original research. It is, however, somewhat remarkable to find the histogenesis of the various nerve elements so much neglected in the earlier investigations. His [19 *et seq*] furnished perhaps the only really substantial contribution to our knowledge regarding the microscopic anatomy of the developing nervous system. His found the spinal cord of the human embryo very suitable for studying the nervous elements, and he distinguished three distinct varieties of these cell elements, viz. :—

(1) *Spongioblasts*, whose processes blend with one another to form a network (the *myelospongium*).

(2) *Germinal cells*, which exhibit active karyokinesis.

(3) *Neuroblasts*, which arise from the division of the germinal cells, and constitute the rudiments of nerve-cells.

For some considerable time I have been engaged in the study of the above cell elements, with the aid of the highest powers of the microscope, in embryos representing all the great vertebrate classes. The degree of magnification which yielded perhaps the best results was that afforded by a $\frac{1}{12}$ immersion lens. One of the first points which arrested attention was the scantiness and peculiar staining properties of the cytoplasm investing the neuroblast-nuclei. These structures were studied more particularly in the chick and embryo frog, the conclusion being that the cytoplasmic investment is at first a faintly-staining perinuclear envelope, which becomes more and more extensive as development progresses. The main object of this paper is to demonstrate that a portion, at least, of this perinuclear investment[1] is a product of the metabolic activity of the neuroblast-nuclei.

The following stains were found most suitable for this research: Mayer's hæm.-alum followed, by eosine, iron-alum hæmatoxylin, the Ehrlich-Biondi mixture, Mann's methyl-blue-eosine, and a mixture of methylene-blue and eosine kindly recommended to me by Dr. Alex. Goodall.

(2) The Assimilative Pole of the Neuroblast-nucleus.

The neuroblast-nuclei of the frog embryo, previous to the tenth day (after fertilisation of the ovum) are very scantily supplied with chromatic elements. The intra-nuclear network is deficient, while the nucleolus stains very faintly (fig. 13), and is on this account frequently difficult to recognise. About the above date many of these nuclei begin to stain very deeply towards one pole (fig. 13). This is in marked contrast to the achromatic character exhibited by the remaining parts of these structures. The late Professor His, in whose laboratory I was at that time working, was one day engaged in study-

[1] This is, to my mind, a much more suitable term than "cytoplasm," or "protoplasm," when referring to the cell body, and will be generally employed throughout this paper.

ing the neuroblast-nuclei of the inner retinal wall in one of my sections from a fifteenth day frog embryo. He was greatly struck with this characteristic arrangement of the chromatic element towards one nuclear pole.[1] He remarked that he had not previously observed this condition, and suggested that it must denote some peculiar property of these nuclei. It was therefore determined to make a careful study of the neuroblast-nuclei at all stages of development, with the result that they were found to exhibit an interesting, and at the same time remarkable, sequence of phenomena.

The neuroblast-nuclei of the frog embryo possess a peculiar relationship to the yolk masses with which the walls of the neural tube are loaded in the early embryonic condition; for it will be readily recognised that the pole which shows the aggregation of chromatic material has in almost every instance a clear achromatic yolk body in close contact with it (figs. 3 and 13). On studying the behaviour of these two structures from the tenth to about the twenty-first days, it will be found that the globules gradually diminish in size until they ultimately disappear altogether, whilst the corresponding nuclei become much larger and at the same time begin to stain very definitely towards the poles which are in such close relationship to the yolk globules. The neuroblast-nucleus in fig. 13 is from the retinal wall of a twelfth day frog embryo, and forms an interesting object for study, for it shows the process of transformation of the achromatic yolk globule into deeply-staining material. The remains of the yolk will be observed lying at the nuclear pole, while within the latter is a well-defined mass which has stained intensely, and is apparently that portion of the ingested globule, which has been newly transformed into nuclear chromatic element. It may be noted here that the neuroblast-nuclei of the cerebral vesicles do not show this unipolar arrangement of the chromatin so strikingly as do those of the retina, although it is very evident in certain regions, such as the developing cerebral hemispheres (figs. 1 and 3). In some Teleostean embryos

[1] This appearance is best demonstrated by the iron-alum-hæmatoxylin stain.

this chromatic aggregation towards one nuclear pole is particularly well marked, as shown in fig. 4, which is a section of the cerebral vesicle of a *Zoarces* embryo. Some of this freshly-acquired chromatic element becomes distributed throughout the bodies of the nuclei as well, and also in the nucleolus, the latter thus staining much more freely than it formerly did (compare figs. 2 and 13).

The most obvious inference to be deduced from these observations is, that the neuroblast-nucleus absorbs the achromatic yolk body, and, after ingesting it, finally stores the product up in the form of a deeply-staining substance. Collateral proof of this is furnished by the fact that those yolk globules which are in relationship with the external poles of the nuclei in the external nuclear layer of the retina become absorbed to a very slight extent only by these nuclei, and thus the characteristic chromatic aggregation towards their external poles is not so marked [4].

It is possible that this collection of deeply-staining material in these nuclei may be due, in part, to the ingestion of pigment from the surrounding tissues. This substance is very abundant in early frog embryos, and may be frequently observed clinging to the yolk globules (fig. 3). It tends to diminish in quantity as development proceeds, so that some of it may possibly be taken up by the neuroblast-nuclei. The author is, however, of the opinion that the major portion of the chromatic material is derived from the yolk.

A study of figs. 1, 3 and 4 will show that those nuclear poles at which the accumulation of chromatic material exists are all pointing in the same direction. Thus, in the walls of the cerebral vesicles, these poles are, as a rule, directed towards the central cavity, while in the retina (fig. 15) they look towards the external limiting membrane, which, of course, lines the cavity of the original optic vesicle, so that the direction is morphologically the same in both instances. Such a definite plan of arrangement of this nuclear pole, taken in conjunction with the fact that it appears to be the chief region of the nuclear wall, through

which the function of yolk ingestion is carried on, would justify one in terming it the *assimilative pole*. This, therefore, is the title which the author has decided to adopt in future when referring to this region of the neuroblast-nucleus in amphibian and teleostean embryos.

The ingestion of the yolk ought, of necessity, to cause an increase in the size of these nuclei, and this is what actually occurs; for these, both in the retina and neural tube of the frog embryo, are much larger at the nineteenth day than they are at the twelfth day. This increase in size, which, it may be noted, occurs during the period that the yolk is being absorbed, is thus most striking. It may be further mentioned that this characteristic enlargement of embryonic nuclei, owing to the ingestion of yolk, is not confined to neuroblasts, for it is found to occur, to a marked degree, in other developing tissues.

The neuroblast-nuclei of higher vertebrates, such as birds (fig. 5), do not possess the above interesting relationship to yolk particles, and thus do not exhibit this peculiar chromatic aggregation at one pole. The blastoderm cells in these higher types are certainly laden with yolk, but the absorption and ingestion of this material in the subsequent stages is through the medium of the vascular system, which is laid down very early in higher vertebrates.

(3) The Nascent or Embryonic and the Mature or Adult Condition of the Nerve-Cell Cytoplasm.

The ingestion by the neuroblast-nuclei of the yolk during the earlier stages denotes a remarkable degree of activity on the part of these structures. More than this, it indicates elaborate preparations for important nuclear metabolic changes which are to be displayed later. The importance of the nucleus as a centre of metabolic activity has been much enhanced by the researches of Hodge [22], Lambert [28], Mann [33], and Vas [46]. These observers have shown that the nucleus of the actively functioning adult nerve-cell exhibits a remarkable sequence of structural changes which will be more fully referred to subsequently.

Miss Huie's researches [25 and 26] on the alterations produced in the gland-cells of *Drosera* by stimulation with food have also an important bearing on the question of nuclear function. In her first paper[1] she remarks: "As a result of an appropriate stimulation of the gland-cells of *Drosera* by food, it is seen that the basophile cytoplasm becomes used up and is represented ultimately by a very scanty eosinophilous plasm. The restoration of the cytoplasm is brought about by the nucleus absorbing food material, metabolising it, and then excreting it into the cytoplasm." Recent researches by Chubb [8] on cell metabolism in the oocyte of *Antedon* are likewise of importance. This observer states,[2] "the chromatin is, therefore, the cell structure, with which the raw food material supplied by the parent organism first comes into relation;" while a little further on he says, "the elaborated food material is passed on from the chromatin, in part to the nucleolus, but mainly to the cytoplasm." The first statement, and part of the second, possess interest when compared with the results chronicled in Section 2 of this paper, where it has been shown that the ingested yolk is stored up as chromatic element, a certain proportion being imparted to the nucleolus. How equally interesting is the last phrase of the second statement will be demonstrated presently. The above researches serve to show that the cell nucleus is the organ in which food material receives its final elaboration, and is then discharged into the cell body to replenish the cytoplasm when occasion demands.

The activity of the nuclear organ will be found very prominently manifested in embryonic nuclei. Witness, for example, the above-described ingestion of yolk, which is to be regarded as partly elaborated food material. The subsequent discharge of this ingested substance from the nuclear organ is no less well marked in embryonic tissues; for the author has previously shown [4] that the delicate processes from the cell elements in the various layers of the amphibian retina are developed as a product of the

[1] P. 423. [2] P. 386.

metabolic activity of the corresponding nuclei, which are, of course, neuroblast-nuclei. Moreover, analogous properties are found to be exhibited by neuroblast-nuclei throughout the whole nervous system.

In the frog embryo, at about the twentieth day, each neuroblast-nucleus becomes surrounded by an ever-widening zone of clear material, which is at first practically achromatic to both nuclear and cytoplasmic stains (acidophile as well as basophile). This is evidently some newly-formed substance which is being added to the original scanty cytoplasm of the neuroblast, and I believe it to be none other than metabolised material which is being discharged from the nucleus, thus forming a faint zone round the latter. Some of the nuclei in fig. 1 show this clear perinuclear envelope, which, in appearance, is not unlike the clear achromatic nuclear material, in which the chromatic filaments of the neighbouring mitotic figures are lying (fig. 1).

The discharge of this achromatic metabolic product is, however, most prominent by far in the region of the assimilative pole, and gradually gives rise to a definite accumulation there, which forms the *rudiment* of the axis-cylinder or axon. Moreover, it is found that, concurrently with the appearance of the above accumulation, the mass of chromatic material within that pole *gradually diminishes and finally disappears.* What apparently happens is, that the stored-up material at the assimilative pole of the neuroblast-nucleus becomes re-transformed, probably by a form of ferment action, into a substance which is profoundly achromatic in the *nascent* condition, and is in this form discharged from that pole. It is thus important to recognise that the axon is always in relation to the assimilative pole, this being obviously due to the previous accumulation of elaborated food material in that region, so that the latter may now be termed the *axon pole.*

The achromatic character of the newly-formed axon rudiment renders its demonstration by photomicrographs extremely difficult, and also prevents a successful study of its various properties under the microscope. It is found, how-

ever, that a somewhat analogous substance is discharged from the external poles of the cone-nuclei in the external nuclear layer of the embryonic amphibian retina, successive emoluments of which gradually accumulate to form the achromatic basal globules which are found in some of the cones (figs. 2, 16, 17). Fig. 2 shows one of the nuclei actually fixed whilst engaged in discharging some of its achromatic metabolic product from the external pole, which, it may be recognised, corresponds to the axon poles of the other retinal neuroblast-nuclei. The wall of the nucleus in this photomicrograph has collapsed somewhat, and, further, the contents of the cone vesicle are apparently in direct continuity with the nuclear matrix. Bernard [1] and the author [5] have previously described a collapsed condition of these cone nuclei as if they had parted suddenly with some of their contents.

This peculiar achromatic nascent substance, which is evidently a characteristic product of all neuroblast-nuclei, very soon undergoes a peculiar process of *re-chromatisation*, in virtue of which it becomes more readily acted upon by both nuclear and cytoplasmic stains. This latter change is, however, only a partial one, and is well seen in the basal vesicles of the retinal cones (fig. 17), which become pervaded by a delicate stainable reticulum after they have been in existence for some time (compare figs. 16 and 17).

The axon-*rudiments* of the optic nerve in amphibians have been already [6] described as consisting of an achromatic metabolic product derived from the neuroblast nuclei in the retinal ganglionic layer (fig. 15). These newly-formed protrusions are, as usual, difficult to recognise on account of their achromatic character, but the successive emoluments gradually form an accumulation from which the pale axon process becomes projected. The latter rapidly undergoes the process of chromatisation just referred to, whereby it becomes more apparent as development proceeds.

The neuroblast-nuclei in the retinal ganglionic layer of amphibia show a peculiar lateral tilting of the assimilative or axon pole. The latter is at first directed outwards in the case of the retinal wall (figs. 13 and 15), and this lateral displacement is found to occur simultaneously with

the appearance of the axon. Whenever this process begins to develop it becomes directed towards the choroidal fissure, with the result that the assimilative pole becomes tilted over *in the same direction*. Two of the nuclei in fig. 15 (above the ×) show this lateral displacement, thus clearly providing further evidence of the close association of the axon rudiment with that pole.

It is a striking fact that the formation of the axon rudiment frequently takes place before the absorption of the yolk at the assimilative pole has been completed. On account of this the globule usually becomes surrounded by the developing axon, as illustrated in fig. 8, which shows neuroblast-nuclei from the spinal cord of a twenty-fifth day frog embryo. One of these (below the ×) shows the yolk completely enclosed by the pale axon, still further proof of the fact that the axon rudiment is associated with the assimilative pole of the neuroblast nucleus. The nucleus below the preceding also shows the presence of a faintly-staining axon in relation to its external pole. The assimilative or axon poles of the neuroblast-nuclei in the spinal cord are thus directed for the most part outwards, instead of towards the central cavity.

On examining the neighbouring neuroblast-nuclei in fig. 8, one is impressed with the scantiness of their investing cytoplasm. Indeed, in several instances they appear to be absolutely devoid of any such investment, so that the accumulation of metabolised material at their axon poles is all the more striking. The comparatively naked appearance exhibited by these nuclei in the early frog embryo, as also the achromatic nature of the axon rudiment, contrast very remarkably with the conditions of the young nerve-cells during the later stages of development. Thus, compare fig. 8 with fig. 9, which is from the spinal cord of a young frog at the close of the metamorphosis. One of the nerve-cells in the latter figure possesses a well-developed axon (γ) which, moreover, has become completely chromatised, and has consequently stained very freely. Note in addition that the axon does not now appear to be related only to the axon pole of the nucleus, but is almost

sufficient in amount to envelop the latter, owing, in part at least, to the gradual accumulation of extruded nuclear material in that region. This enveloping process is completed by the time the adult condition is reached, the nucleus becoming ultimately surrounded by an extensive investment, a large proportion of which is, like the axon rudiment, apparently secreted by itself. Some of the neighbouring nuclei in fig. 9 will be observed to possess a very feebly-formed axon even at this late stage of development (β). One can thus readily recognise in fig. 9 three distinct phases of formation of young nerve-cells from the neuroblast-nuclei (a)—*the* a, β *and* γ *phases.*

The neuroblasts of the chick will be found to possess a developmental history similar to those of the frog, and illustrate well the same stages of transition, which have just been described in the preceding paragraph. The young fourth day neuroblast-nuclei show the faintly-staining axon as the most prominent process (fig. 5). As development advances the nucleus secretes more and more material in order to promote the growth of the axon, whose point of "attachment" thus becomes broadened, and gradually encircles the nucleus, exactly as in the frog embryo (fig. 9). The condition of the neuroblasts in the spinal cord of a seventh day chick is shown in fig. 10. The one lettered (β) shows a well-formed chromatised axon in relation to its axon pole, while that lettered (a) is lying within a clear space, and appears to be still devoid of both investment and processes—*the* a *and* β *phases.*

Two later stages of development of nerve-cells from neuroblasts in the chick are illustrated in figs. 11 and 12. In fig. 11, which is from the spinal cord of a fourteenth day chick, the metabolic product is still accumulating around the axon poles of the nuclei, the latter thus possessing a characteristic excentric position in the embryonic nerve-cells, a relation which, it may be stated, was observable in all the vertebrate types examined. The appearance just mentioned seems to be best explained by the fact (already referred to) that the discharge of the nuclear product occurs chiefly from the axon pole. Hence the persistent accumu-

lation of extruded material around that pole. The perinuclear investment of the nerve-cells in fig. 11 now exhibits dendritic processes, which are thus secondary to the formation of the axon—*the γ phase.*

Contrast the appearance of the cells in fig. 11 with fig. 12, which is from the spinal cord of a chicken a few hours after hatching. Two decided points of difference will be observed; for the nucleus, in one case at least, has now assumed its permanent position in the centre of the nerve-cell, while it will also be observed to be spherical in shape, as found in the adult condition of the cell. The adoption of the spherical outline by the adult cell-nucleus is probably due to the fact that the products of metabolism are now discharged uniformly from every part of the nuclear wall. This is in striking contrast to the bipolar embryonic nucleus, the shape of which is possibly influenced by the fact that the discharge of metabolised material is mainly polar.

The neuroblast-nuclei in the spinal cord of the chick exhibit striking structural changes as development advances, thus furnishing further proof of their great metabolic activity. In the early stages the nuclear chromatin is dispersed more or less evenly throughout the bodies of these structures as seen in fig. 5. A glance at figs. 10, 11 and 12, however, shows that there is a tendency to a heaping together of the chromatic elements into one or more large irregular masses during the subsequent developmental stages, leaving the rest of the nucleus comparatively free from chromatin.

A study of fig. 6, which shows the condition of the neuroblasts in the neopallium of a fourteenth day chick, will be found most interesting. Note particularly that, even at this comparatively late stage of development, they exist practically as nuclei imbedded in myelospongium, their axon processes being entirely absent. Contrast the appearance of these neuroblasts (to be referred to subsequently as the *a*-neuroblasts) with that presented by those in fig. 11. The latter are from the anterior cornu of the spinal cord of the same embryo, and show a considerable degree of

development. A similar difference in the condition of the neuroblasts from corresponding regions of the frog embryo at the end of the metamorphosis is also readily observable.

It is a well-recognised fact that within the spinal cord of the lower vertebrate classes are located a large number of important nerve centres, while the neopallium of the cerebral hemispheres in the same animals appears to be very feebly endowed with functions. This is evidenced even in the embryos of these animals (*e.g.*, the frog and chick) by a marked degree of development of nerve-cells from the neuroblasts of the spinal cord, and a correspondingly feeble condition of growth of the neuroblasts in the neopallium. Indeed, those in the latter site seem to preserve their primitive embryonic character even in the adult.

Contrast these, again, with the neuroblasts shown in fig. 7 which are from the pyramidal cell layer of the cerebral hemisphere of a rat embryo. It will be observed that at this early stage these important cell elements simply look like a mass of nuclei closely arranged together. These nuclei, however, gradually acquire an investment which first shows round their axon (*i.e.*, their internal) poles, just as in the case of the young nerve cells in the spinal cord of the chick and embryo frog. This observation comes to possess great interest when it is recollected that the cortical cells in mammals attain to a higher degree of evolution than those of lower vertebrates, obviously in order to enable them to undertake the important functions which become transferred from the lower brain centres.

All the above-described neuroblasts which have been chosen from the various regions of the developing central nervous system in vertebrate embryos indicate that their original scanty cytoplasm takes little part in the formation of the axon rudiment, the latter, as also a considerable part of the protoplasm of the future nerve-cell, being a product of nuclear metabolism. Provision seems to be first made for the formation of the axon. This ought not to cause surprise, seeing that it is such an essential element of the neuron.

Burckhardt [2] is the only observer, so far as can be ascertained, who has drawn attention to the above intimate association of the axis-cylinder with the neuroblast-nucleus. His paper deals with a study of the neuroblasts in the embryonic spinal cord of *Triton* (it may be noted here that the neuroblast-nuclei of amphibian embryos show the nuclear origin of the axon to best advantage). On page 146 of his paper he states: "dagegen ist es mir gelungen Axencylinder von diesen Kernen ausgehen zu sehen, und zwar sehr zarte Axencylinder die nur bei starken Vergrösserungen können wahrgenommen werden."

With the continued extrusion of more and more nuclear material, the original relationship of the axon to the nucleus must, of necessity, become disguised; but many observers have shown that, even in the adult nerve-cell, it may be traced for a considerable distance into the substance of the cytoplasm in the direction of the nucleus. Such an appearance has been described by Lenhossék [29] in the spinal ganglion cells of the frog, by Daae [9] and Flemming [13] in the spinal ganglion cells of mammals; also by Smirnow [45] and Dehler [10] in the sympathetic ganglion cells of amphibia, and by Dogiel and Tumänzew [12] in the cells of the cardiac ganglia.

It will now be apparent that these above observations on the behaviour of the neuroblast-nucleus constitute a change from the views which are held with regard not only to the ontogeny of the nerve-cell, but also the life history and morphology of cells in general. It has been generally supposed that, since all the cells which constitute the organism are derived from the ovum, the cytoplasm of each cell must possess a share, however small, of the original deutoplasm. The results of this research tend to show that, in the central nervous system, the remains of the deutoplasm are probably represented by the inert myelospongium network, in which some of the nuclei remain imbedded, thus forming the spongioblasts, which are the rudiments of the neuroglia cells, while others become free in the meshwork as the neuroblast-nuclei. The actively functioning nerve-cells thus possess a much more interesting life history than

the neuroglia, for they all appear to begin their existence as nuclei. No one will deny the fact that the protoplasm of nerve-cells must possess properties quite distinct from those of the more passive supporting tissue, these specific properties being imparted to the former by the neuroblast nucleus, from which a large portion of it is derived.

The chromatisation of the perinuclear envelope of neuroblasts takes place just as in the case of the basal achromatic globules in the amphibian cones. It constitutes an important phase in the life history of the nerve-cell investment, for its represents the transition from its nascent or immature to its more mature condition. The chromatisation of the axon and perinuclear envelope of the embryonic nerve-cell does not affect the whole uniformly, just as in the cone globules, but is confined chiefly to a fine longitudinal fibrillation which is very well demonstrated by the iron-alum hæmatoxylin stain (figs. 9, 11 and 12). The origin of the neuro-fibrillary network and the fibrils which are so prominent a feature of nerve-cells and their processes, and about which so much has been written, is thus explained.[1]

It will now be observed that the neuroblasts in lower vertebrates exhibit a remarkable train of phenomena during the progress of development. Thus their nuclei ingest partly elaborated material in the form of yolk, and store it up as chromatic element. The latter becomes in course of time transformed into a substance which is achromatic in the nascent condition, and is in this form discharged from the nucleus. This nascent achromatic material is in its turn re-chromatised, so that we are provided with a peculiar alternation of chromatic and achromatic phases of nuclear material. The various steps of this transformation may be represented as follows:—

(1) Ingestion by the nuclei of the achromatic yolk globule.

(2) Storage of the product in the nucleus as chromatic material.

[1] The formation of the Nissl bodies is also brought about by localised areas of chromatisation occurring in extruded nuclear material. Their histogenesis will be described in a subsequent communication.

(3) Discharge of the latter from the nucleus as achromatic material.

(4) Re-chromatisation of the latter, in its turn, outside the nucleus.

This alternation of the chromatic and achromatic condition of nuclear material is not surprising, for it may be observed in the behaviour of the lateral branches of the chromatin filaments, which, as is well known, become temporarily achromatic during mitosis. Note, in addition, how the activity of nuclear division manifests itself by an exaggeration or intensification of the reaction of its chromatic and achromatic elements towards staining agents. Thus, the chromosomes stain very intensely, while the so-called nuclear membrane, which is only comparatively achromatic in the resting condition, becomes absolutely so during the middle phases of mitosis.

(4) Changes exhibited by the Neuroblast-nuclei, as Evidence of their Metabolic Activity.

The *structural* changes exhibited by the actively functioning neuroblast-nuclei have been already described in the two preceding sections. These nuclei also exhibit alterations in *size* as evidence of the extrusion of their metabolic product. These changes are not always apparent. They are seen to a marked extent, however, in the retina, where they are found to be also progressive in character. The accompanying series of illustrations of the retinæ of frog embryos (all of exactly the same magnification) demonstrate this phenomenon very well. For example, fig. 15 shows the condition of the inner retinal wall in a nineteenth day frog embryo. Many of the nuclei are actively engaged in giving off their achromatic product. As a consequence of this, it is found that by the thirty-fifth day a marked *diminution* has taken place in the size of these nuclei (fig. 16). This reduction in size is shown on comparing figs. 15 and 16, and is not due to a multiplication of the nuclei, for there is no increase in their number, as compared with the nineteenth day. The reduction in size is

not so evident during the later stages of development. This is, however, to be expected, seeing that the formation of the protrusions is not so marked in these stages; but is, on the other hand, concomitant with the diminution in size of the nuclei between the nineteenth and thirty-fifth days.

The nuclei in the retinal ganglionic layer of the adult frog practically retain their embryonic character, that is to say, they do not become completely invested by cytoplasm, the result being that their various processes appear to pass directly from them (fig. 18). The corresponding nuclei in the mammalian retina, however, become surrounded by a definite investment from which the various processes pass (fig. 19).

The ganglion habenulæ is another region in which evidences of the existence of the achromatic function are denoted by a reduction in the size of the nuclei. A comparison of figs. 20 and 21 will demonstrate this fact, for the nuclei in the latter fig. (ganglion habenulæ of a young frog) exhibit a striking degree of diminution in size when compared with those of fig. 20, which are from the same region in a fifteenth day frog embryo. A similar diminution is also observable in the cerebral hemispheres of the frog embryo.

It will be found that a reduction in the size of these neuroblast-nuclei is only present in regions, such as those cited, where these structures preserve their embryonic character, as will be fully described in Section 5, and it is probably to be explained by the fact that their achromatic function is in excess of their assimilative power for food material. In other localities of the developing central nervous system, such as the anterior cornu of the spinal cord in birds and amphibians, the nuclei show great activity (figs. 8 to 12). They therefore tend to become enlarged, like the nuclei of adult nerve-cells, when called upon to perform extra work; as shown by the researches of Mann [33] and Vas [46]. The assimilative power of the nuclei in the last-mentioned region thus appears to be in excess of their achromatic function, and thus they exhibit an increase in size. In this respect they differ from those

neuroblast-nuclei which tend to preserve and maintain their embryonic condition.

(5) The *a*-, *β*- and *γ*-Neuroblasts.

It will be observed from the foregoing description that one can readily recognise three distinct types of neuroblasts in vertebrate embryos. For these the titles of *a*-, *β*- and *γ*-neuroblasts have been adopted.

The name of *γ*-neuroblast has been conferred on those whose nuclei exhibit great activity, both in regard to their assimilative and achromatic functions, while in the bipolar embryonic condition. These nuclei thus become enclosed by a more or less extensive investment, and are thereby qualified to pass from the embryonic to the more mature or adult stage. Whenever the development of the young nerve-cell is complete, the nucleus assumes the spherical adult condition (fig. 12). This type is so readily recognisable that a further description will be unnecessary.

The title of *β*-neuroblast has been adopted for those which become very scantily endowed with a perinuclear investment, and, in addition, retain their embryonic character more or less. They preserve, however, their actively-functioning properties in the adult. Various examples of regions in which the neuroblasts retain their embryonic character have just been cited in Part 4, such as the retina and ganglion habenulæ of the frog; and it is of interest to recognise that the persistence of this condition is very widespread throughout vertebrates, but is most evident in the lower classes, *e.g.*, amphibians and fishes. Take for example the spinal ganglion cells of teleosteans (fig. 14). These retain their embryonic bipolar character owing to the fact that the perinuclear material is collected mainly at the poles of the nuclei. On ascending the vertebrate scale, however, the protoplasmic element becomes more and more marked, with the result that the bi-polar condition of these cell elements is gradually masked, until ultimately the two processes fuse together, and thus come to possess a single stem of origin. A further example of retention of

this embryonic character may be recognised in fig. 21, which shows the primitive condition of the nerve-cells in the ganglion habenulæ of a young frog.

The internal nuclear layer of the retina possesses a special interest in this connection, for it is found that the cell elements of this region in all vertebrates retain the β-type throughout life (figs. 18 and 19). Their nuclei thus preserve the characteristic bipolar embryonic condition, and from their poles the external and internal processes pass, just as in the spinal ganglia of teleosteans.

The nuclei of the β-neuroblasts have thus deficient powers of secreting their metabolic product, but more especially of assimilation. As a result they exhibit a progressive diminution in size during embryonic life (as shown in Section 4), while even in the adult they possess a very scanty perinuclear envelope, and thus preserve their primitive embryonic condition more or less.

The α-neuroblasts are found widely distributed throughout the whole central nervous system. Their special characteristics will be readily recognised in figs. 6, 8, 9, 10 and 12. They appear to be simply neuroblast-nuclei which are very small, practically devoid of investment, and lying free in the myelospongium network. In the above figures they are shown in striking contrast with the γ-neuroblasts near which they chance to lie. The nuclei of these α-neuroblasts, like those of the β-type, exhibit a progressive diminution during embryonic life. Further, they seem to retain their primitive character throughout life. It is somewhat difficult to understand what function they subserve. A possible explanation is, that they form a reserve for the supply of new nerve-cells. They may thus tend to develop into activity, and become transformed into fully-developed and actively-functioning nerve-cells, when special demands are made upon the region in which they lie. This statement is supported by the fact that the neuroblasts in the neopallium of the chick mostly belong to the α-type (fig. 6). This region of the brain is apparently devoid of function in birds, but has most important brain centres transferred to it in the higher mammals. This transference

is probably effected by a lighting up of activity in these *a*-neuroblasts, whereby they become transformed into fully-developed nerve-cells. Further, it is recognised by many authorities that the life history of cells in general may be shorter than that of the individual, a statement which refers probably to nerve-cells as well. The *a*-neuroblasts may thus constitute a store of embryonic nerve-cells, which can be drawn upon when occasion demands.

On studying transverse sections of the embryonic and the adult spinal cord, one is struck with the small proportion of *adult* nerve-cells, as compared with the number of neuroblasts. The enumeration of the neuroblasts in any transverse section would turn out a very difficult and tedious operation. Capobianco [7], however, undertook the task of calculating the number of neuroblasts in the spinal ganglion of a cat embryo, comparing this with the number of nerve-cells in two ganglia of the adult.[1] He found the proportion of mature nerve-cells to neuroblasts in the two cases to be 1 to 2·83 and 1 to 3·20. I would explain this apparent diminution as due, partly, at least, to the retention by these *a*-neuroblasts of their embryonic character, so that they might quite readily be mistaken for neuroglia-nuclei (figs. 9 and 12). Fragnito's [14] explanation of the apparent diminution in numbers of the neuroblasts during development will be referred to in Section 6.

The existence of these *a*-neuroblasts supports the previously expressed contention that nerve-cells must begin their life history as nuclei. It is, further, of interest to note that all three types of neuroblast represent distinct stages in the ontogeny of nerve-cells. The *a*-neuroblast represents the first stage, from which further development brings us to the β-neuroblast, the latter forming the second stage. Lastly, we obtain the most highly-evolved stage, as represented by the γ-neuroblast, from which the fully-developed nerve-cell is obtained. These three stages are illustrated in fig. 9, in the centre of which are seen two well-formed γ-neuroblasts. Below these, two

[1] For particulars of this paper I am much indebted to Dr. R. G. Rows.

β-neuroblasts may be observed, with faintly-staining axons associated with their axon poles (β), while to the right of the γ-neuroblasts are two small neuroblast-nuclei which are apparently devoid of investment, and thus belong to the a-type (a).

(6) The Presence of Nuclear Derivatives in the Cytoplasm of Nerve-Cells.

Held [16 *et seq.*] was one of the first to show that the Nissl bodies in the nerve-cells of vertebrates consist of a nucleo-proteid. He based his results mainly on the resistance which these bodies offer to artificial digestion, and on the fact that they contain phosphorus in their molecule. Rohde [39 *et seq.*] has also studied the relation of the nucleus to the cytoplasm of the nerve-cell. He describes the migration of those masses of nuclear chromatin which constitute the secondary nucleoli, into the cell-body to become the Nissl spindles. Holmgren [23] also expresses the conviction that the nuclei of nerve-cells extrude their chromatin into the cytoplasm. His observations were made on the spinal ganglion cells of *Lophius*. In these he describes a characteristic migration of small masses of chromatin out of the nucleus to form the Nissl bodies. He was able to confirm these results in a later paper [24]. Scott's researches on this subject are also of interest [43]. This observer has been able to trace the origin of the Nissl bodies from the chromatin of the germinal cells in the embryonic neural tube. Thus he states: "The three nuclein compounds of the adult nerve-cell, the Nissl granules, the nucleolus and the oxyphile nuclear substance are derived from the chromatin of the nucleus of the germinating cell. This chromatin divides into two parts, each containing iron and phosphorus, but the one is oxyphile, and remains in the nucleus, while the other is basophile and diffuses into the cell body, and becomes the Nissl granules." Scott casts doubt on Holmgren's assertion that the nuclear chromatin is extruded in the form of small particles, and suggests, instead, that it may be given

off in solution. He points out, however, the necessity for further investigation to determine this point. In a more recent paper Scott [44] shows that substances of a nature similar to the Nissl bodies of nerve-cells occur in certain gland-cells.

From the results chronicled by these above observers no reasonable doubt can be entertained that the cytoplasm of the nerve-cell is, in part, at least, derived from the corresponding nucleus. Scott's observations regarding the origin of the Nissl bodies from the nuclear chromatin are somewhat similar to the results of the present research. Thus it has been shown in Part 3 that a great part of the nerve-cell cytoplasm, and probably also the Nissl bodies, are derived from the nuclear chromatic element. The latter is transformed into a nascent achromatic substance, which is then immediately extruded from the nucleus. This material very soon, however, undergoes a process of re-chromatisation, and thus both the neurofibrillary network and the Nissl bodies are produced. Therefore the nuclear chromatin is probably not discharged in the form of granules as Rohde and Holmgren have described, but in the form of fluid, as Scott suggests.

The results obtained by Fragnito [14 *et seq.*] with reference to the development of nerve-cells in the chick and those of Capobianco [7] in embryos of the cat and of man, are also of interest in comparison with the present research. The former finds that at the beginning of the seventh day of incubation the neuroblasts in the anterior cornu of the cord become arranged into groups (cell colonies). He divides the former into primary neuroblasts from which the permanent cell nucleus is derived, and secondary neuroblasts which become transformed into the various constituents of the adult cell protoplasm; Capobianco obtains analogous results in the embryos examined by him. Fragnito and Capobianco describe various stages of this transformation of these secondary neuroblasts, such as loss of contour and fusion of the various elements. The former observer finds, further, that the axis-cylinder and the dendrites are similarly formed from the fusion of

transformed cells. These results have been confirmed in the main by Kronthal [27].

I have observed a close grouping of the above neuroblasts, which is certainly suggestive of a tendency to a fusing of these elements, but so far I have been unable to satisfy myself definitely of the actual occurrence of this in any of the specimens examined during this research.[1] According to Fragnito and Capobianco, then, practically the whole of the nerve-cell cytoplasm must be directly nuclear in origin, the essential point of difference from the results of the present research resting in the fact that this cytoplasm is plurinuclear in origin instead of mononuclear, which I hold it to be.

Fragnito's classification into primary and secondary neuroblasts is also of interest, for it has been shown in Part 5 of this paper that three (α, β and γ) types of these structures may be recognised. The fate of Fragnito's secondary neuroblasts is, however, different from that of the above α and β types, so that it is impossible to draw a distinct analogy between them.

It is important also to refer here to the behaviour of the nucleus of the nerve-cell during Nissl's [35] degeneration. In this condition it is found that the cell nucleus takes up an excentric position, and becomes oval in shape, thus appearing to revert to the primitive embryonic condition.

(7) The Behaviour of the Neuroblast-nuclei compared with that of the Nuclei of Actively-Functioning Nerve-Cells.

The effects of fatigue upon nerve-cells have been investigated by, among others, Hodge [22], Lambert [28], Mann [33], and Vas [46]. Although the individual results of these observers differ somewhat in detail, the main con-

[1] Since this paper was sent to press, I have had an opportunity of examining sections of the cord of mammalian embryos and of the chick, prepared by Drs. D. Orr and R. G. Rows. In many of these one could recognise a definite aggregation of the neuroblast-nuclei into colonies, together with a loss of contour which were certainly strongly suggestive of a process of fusion of the individual elements.

clusions arrived at point to the fact that during activity the nucleus enlarges slightly; but with the advent of fatigue it becomes much reduced in size, and even shrunken. Its chromatin at the same time becomes much diminished in quantity, due apparently to its having become transformed into another substance, the latter being then extruded freely in order to replenish the protoplasm.

It is remarkable how closely the phenomena which are exhibited by the fully-developed nerve-cells during activity and fatigue are simulated by the neuroblast-nuclei in certain regions, such as the retina, during development. For example, the nuclei of the retinal ganglionic layer in the frog embryo illustrate this exceedingly well, as is clearly shown in figs. 15 and 16. In the early stages there is an increase in the size of the nuclei due to their absorbing the digested yolk. This is probably a provision to allow them to undertake the important function of secreting their metabolic product which is so soon to follow. This metabolism of these nuclei is evidenced by a progressive diminution in their size, together with a using up of the accumulated chromatic material; these processes continue throughout development, but are most apparent in the early stages, during which period, it may be noted, most of the processes are formed. This diminution is so gradual that these nuclei rarely exhibit the shrunken appearance which is so marked a feature of fatigue; but, on the other hand, it was shown that certain of the cone-nuclei in the amphibian retina extrude their achromatin so suddenly and rapidly that many become quite collapsed (fig. 2).

This close correspondence between the behaviour of these embryonic nuclei and that of the fully-developed functioning nuclei is most striking and suggestive. The whole train of phenomena, both during development and fatigue, prove clearly that the nucleus not only gives origin to a large part of the protoplasm of the future nerve-cell, but also furnishes a fresh supply of material to replenish that protoplasm when its properties have become impaired or exhausted from the continued exercise of its function.

It thus seems evident that the nucleus must exert an important influence, not only on the development, but also on the subsequent life history of the nerve-cell. The results of this research have, therefore, an important bearing on Waller's views regarding nerve degeneration [48]. The Wallerian law, as usually formulated, affirms that an axon, when cut off from its nutritive centre, which is a nerve-cell, soon begins to exhibit degenerative changes. The results of the present research show, however, that the nucleus of the nerve-cell is the real nutritive centre. It is, therefore, obvious that an important modification in our present acceptation of the Wallerian law will be necessary, so that the latter, as now constituted, would read somewhat as follows: An axis-cylinder, when cut off from its nutritive centre, which is the *nucleus* of a nerve-cell, soon begins to show degenerative changes.

The question of the histogenesis of nerve-fibres is dealt with in another communication.[1] The further growth of the axis-cylinder will be found fully described and discussed there.

The results detailed in this paper are the outcome of research performed under the terms of tenure of a Carnegie Fellowship. The work was begun in the Anatomy Department, United College, University of St. Andrews, and completed in the Anatomy Department, University of Manchester. I wish here to express my thanks to Professor Musgrove and Professor Young for their kindness in offering me every facility and encouragement during its progress, as also to the Executive Committee of the Carnegie Trust for so liberally supplying the necessary funds to cover the incidental expenses of the research. I desire also to express my gratitude to Dr. Nöel Paton for the use of the microphotographic apparatus in the laboratory of the Royal College of Physicians, Edinburgh, as also to Mr. E. Watson for kindly taking the microphotographs from which all the figures, except 1, 2, 4 and 13, have been prepared. For the latter I am indebted to Mr. Richard Muir.

[1] In the *Journal of Anatomy and Physiology* for October, 1906.

(8) Summary of Results.

(1) The scanty cytoplasmic investment which the neuroblasts possess during the early developmental stages takes little part in producing the abundant cytoplasm of adult nerve-cells.

(2) The latter is to be regarded partly as a product of the metabolic activity of the neuroblast-nuclei during embryonic life.

(3) One of the earliest indications of this metabolic activity is shown in lower vertebrates (*e.g.*, fishes and amphibians) by an ingestion of yolk particles at one definite pole of the nuclear wall. For this the title of *assimilative pole* has been adopted.

(4) The ingested yolk is elaborated within the nucleus and stored up as chromatic material which first shows near this pole.

(5) The ingestion of the yolk is further evidenced by a progressive increase in the size of the nuclei, which occurs during the period that the above absorptive process is going on.

(6) The rudiment of the axis-cylinder process arises in the form of successive extrusions of nuclear achromatic substance from the assimilative pole of the neuroblast-nucleus. This pole thus becomes the *axon pole.*

(7) It is to be clearly understood that the term *achromatic* is applied throughout this paper to a fluid substance which is nuclear in origin, and is, in the nascent condition, strongly resistant to the action of all colouring agents. This term is therefore applied in contradistinction to the chromatic or staining elements of the nucleus. It is possible that several distinct substances may be included under this title of achromatin; but from its very nature it has as yet defied attempts at ascertaining its composition by means of microchemistry.

(8) The assimilative or axon pole of the neuroblast-nucleus has always a definite direction. Thus it looks towards the ventricular cavity in the cerebral hemispheres,

and forwards as well as outwards in the anterior cornua of the spinal cord.

(9) Not only the axon rudiment, but also a great part of the cytoplasm of the future nerve-cell is produced from the neuroblast-nucleus, owing to the continued exercise of this *achromatin function*.

(10) The nuclear metabolic product is extruded mainly from the axon pole. This would account both for its gradual accumulation in this region, and also for the excentric position of the nucleus in the embryonic nerve-cell.

(11) The material which is given off from the neuroblast-nucleus is achromatic only in the *nascent* condition. It very soon, however, undergoes a characteristic process of re-chromatisation which affects the extruded perinuclear substance in a definite manner, and gives rise to the neuro-fibrillary network and the Nissl bodies.

(12) The neuroblast-nuclei exhibit structural changes as evidence of their metabolic activity. The most striking is a disappearance of the accumulated chromatic material from the axon pole, which occurs during the period that the axon rudiment is being given off. The chromatic element is thus re-transformed into nascent achromatic element, in which condition it is discharged from the nucleus.

(13) In some regions (the retina, cerebral hemispheres and ganglion habenulæ) of lower vertebrates, the neuro-blasts exhibit, in addition, a marked reduction in size during the period that this achromatic element is being discharged.

(14) Three types of neuroblasts may be recognised. For these the names of α-, β- and γ-neuroblasts have been adopted.

(15) The α-neuroblasts retain their embryonic character more or less. They probably form a reserve of young nerve-cells.

(16) The β-neuroblasts become invested by a very scanty envelope, their processes thus appearing to pass directly from the nuclei.

(17) The γ-neuroblasts become transformed into actively

functioning nerve-cells, and become endowed with an abundant investment which forms the adult cell-cytoplasm.

(18) It is important to note that nerve-cells begin their life history as the α-type of neuroblast, and pass successively through the β- and γ-types.

(19) Several observers have shown that the cytoplasm of nerve-cells is rich in nuclein compounds. This seems to suggest that a part of it at least is derived from the nucleus, as shown in this research.

(20) The nucleus not only gives part origin to the protoplasm of the nerve-cell, but also furnishes a supply of fresh material to replenish the latter, when occasion demands, throughout the life history of the individual. The nucleus is thus the nutritive centre for the nerve-cell.

(21) It is thus obvious that a modification in our present acceptation of the Wallerian law of degeneration will be necessary. The latter ought therefore to read somewhat as follows: An axon, when cut off from its nutritive centre, *i.e.*, the *nucleus* of a nerve-cell, soon exhibits degenerative changes.

(9) Literature.

[1] Bernard, H. M. "Studies in the Retina," part ii. *Quart. Jour. Micr. Sci.*, vol. xliv., 1901.

[2] Burckhardt, R. "Histologische Untersuchungen am Rückenmark der Tritonen." *Archiv. für Mikros. Anat.*, Bd. xxxiv., 1889.

[3] Cameron, J. "The Development of the Retina in Amphibia," part i. *Journ. Anat. and Phys.*, vol. xxxix., 1905.

[4] Cameron, J. "The Development of the Retina in Amphibia," part ii. *Journ. Anat. and Phys.*, vol. xxxix., 1905.

[5] Cameron, J. "The Development of the Retina in Amphibia," part iii. *Journ. Anat. and Phys.*, vol. xxxix., 1905.

[6] Cameron, J. "The Development of the Optic Nerve in Amphibians." *Studies from the Anat. Depart., The Victoria University of Manchester*, vol. iii.

[7] Capobianco, F. "Ulteriori Ricerche sulla Genesi delle Cellula nervosa." *Annali di Nevrolog.*, Anno. xxiii., Fasc. 1 and 2.

[8] Chubb, G. C. "The Growth of the Oocyte in *Antedon*: a Morphological Study in the Cell Metabolism." *Proc. Roy. Soc.*, vol. lxxvii., 1906, series B.

[9] Daae, Hans. "Zur Kenntniss der Spinalganglienzellen beim Säugethier." *Archiv. für Mikros. Anat.*, Bd. xxxi., 1888.

[10] DEHLER, ADOLPH. "Beitrag zur Kenntniss vom feineren Bau der sympathischen Ganglienzelle des Frosches." *Archiv. für Mikros. Anat.*, Bd. xlvi., 1895.

[11] DOGIEL, A. S. "Zur Frage über den feineren Bau des sympathischen Nervensystems bei den Säugethieren." *Archiv. für Mikros. Anat.*, Bd. xlvi., 1895.

[12] DOGIEL, J., AND TUMÄNZEW. "Zur Lehre über das Nervensystem des Herzens." *Archiv. für Mikros. Anat.*, Bd. xxxvi., 1890.

[13] FLEMMING, W. "Ueber den Bau der Spinalganglienzellen bei Säugethieren, und Bemerkungen über den der centralen Zellen." *Archiv. für Mikros. Anat.*, Bd. xlviii., 1895.

[14] FRAGNITO, O. "Lo Sviluppo della Cellula nervosa nel Midollo spinale di Pollo." *Ann. di Nevrolog.* 1902, f. 3.[1] Abstract in *Review of Neur. and Psych.*, vol. 1, No. 1.

[15] FRAGNITO, O. "Per la Genesi della Cellula nervosa." *Anat. Anz.*, Bd. xxii., 1902.

[16] HELD, HANS. "Beiträge zur Struktur der Nervenzellen und ihrer Fortsätze." *Archiv. für Anat. und Phys., Anat. Abth.*, 1895.

[17] HELD, HANS. "Beiträge zur Struktur der Nervenzellen und ihrer Fortsätze." *Archiv. für Anat. und Phys., Anat. Abth.*, 1897.

[18] HELD, HANS. "Beiträge zur Struktur der Nervenzellen und ihrer Fortsätze. Dritte Abhandlung." *Archiv. für Anat. und Phys., Anat. Abth.*, 1897 (supp.).

[19] HIS, WM. *Anatomie menschlicher Embryonen*, Leipzig, 1880-85.

[20] HIS, WM. "Die Neuroblasten und ihre Entstehung im embryonalen Mark." *Archiv. für Anat. und Phys., Anat. Abth.*, 1889.

[21] HIS, WM. "Histogenese und Zusammenhang der Nervenelemente." *Archiv. für Anat. und Phys.*, 1890 (supp.).

[22] HODGE, C. F. "A Microscopical Study of Changes due to Functional Activity in Nerve-Cells." *Journal of Morph.*, vol. vii., 1892.

[23] HOLMGREN, E. "Zur Kenntniss der Spinalganglienzellen von *Lophius piscatorius*, Lin." *Anat. Hefte*, 38, 1899.

[24] HOLMGREN, E. "Studien in der feineren Anatomie der Nervenzellen." *Anat. Hefte*, 1900, Bd. xv., Heft 1.

[25] HUIE, LILY H. "Changes in the Cell-organs of *Drosera rotundifolia* produced by Feeding with Egg-albumen." *Quart. Jour. Micr. Sci.*, vol. xxxix., 1897.

[26] HUIE, LILY H. "Further Study of Cytological Changes produced in *Drosera*." *Quar Jour. Micr. Sci.*, vol. xlii., 1899.

[27] KRONTHAL, P. Von der Nervenzelle und der Zelle im Allgemeinen, Jena, 1902.

[28] LAMBERT, F. "Note sur les Modifications produites par l'Excitation électrique dans les Cellules nerveuses des Ganglions sympathiques." *Compt. Rend.*, 1893, No. 31.

[29] LENHOSSÉK, M. VON. "Untersuchungen über die Spinalganglien des Frosches," *Archiv. für Mikros. Anat.*, Bd. 26, 1886.

[30] LENHOSSÉK, M. VON. "Centrosom und Sphäre in den Spinalganglienzellen des Frosches," *Archiv. für Mikros. Anat.*, Bd. 46, 1895.

[1] The author is much indebted to Dr. Forbes Robertson for having drawn his attention to this paper.

[31] LENHOSSÉK, M. VON. "Die Entwickelung der Ganglienanlagen bei dem Menschlichen Embryo," *Archiv. für Anat. und Phys., Anat. Abth.*, 1891.

[32] MANN, G. "Structure, Staining Reactions and Functions of Nuclei," *Proc. Brit. Assoc., Section D*, 1892.

[33] MANN, G. "Histological Changes induced in Sympathetic, Motor and Sensory Cells by Functional Activity," *Jour. Anat. and Phys.*, vol. xxix., 1894.

[34] MUHLMANN, M. "Weitere Untersuchungen über die Veränderungen der Nervenzellen in verschiedenem Alter," *Archiv. für Mikros. Anat.*, Bd. 58, 1901.

[35] NISSL, F. "Ueber experimentell erzeugte Veränderungen an den Vorderhornzellen des Rückenmarks bei Kaninchen," *Allgem. Zeitsch. f. Psych.*, Bd. 48, 1892.

[36] ONODI, A. D. "Ueber die Entwickelung des sympathischen Nervensystems," *Archiv. für Mikros. Anat.*, Bd. 26, 1886.

[37] ONODI, A. D. "Ueber die Entwickelung des sympathischen Nervensystems. Zweiter Theil." *Archiv. für Mikros. Anat.*, Bd. 26, 1886.

[38] RETZIUS, G. "Untersuchungen über die Nervenzellen der cerebrospinalen Ganglien und der übrigen peripherischen Kopfganglien mit besonderer Rücksicht auf die Zellenauslaüfer," *Archiv. für Anat. und Phys., Anat. Abth.*, 1880.

[39] ROHDE, E. "Ganglienzelle und Neuroglia," *Archiv. für Mikros. Anat.*, Bd. 42, 1893.

[40] ROHDE, E. "Ganglienzelle, Axencylinder, Punctsubstanz und Neuroglia," *Archiv. für Mikros. Anat.*, Bd. 45, 1895.

[41] ROHDE, E. "Ganglienzellenkern und Neuroglia," *Arch. für Mikros. Anat.*, Bd. 47, 1896.

[42] SCHULTZE, H. "Mikroskopische Studien über die Struktur der Nervenfaser und Nervenzelle der Wirbelthiere," *Archiv. für Anat. und Phys., Anat. Abth.*, 1878.

[43] SCOTT, F. H. "The Structure, Microchemistry and Development of Nerve-Cells," *Trans. Canad. Instit.*, vol. vi.[1]

[44] SCOTT, F. H. "On the Metabolism and Action of Nerve-Cells," *Brain*, vol. xxviii., parts 111 and 112, 1906.

[45] SMIRNOW, A. "Die Struktur der Nervenzellen im Sympathicus der Amphibien," *Archiv. für Mikros. Anat.*, Bd. 35, 1890.

[46] VAS, F. "Studien über den Bau des Chromatins in der sympathischen Ganglienzelle," *Archiv. für Mikros. Anat.*, Bd. 40, 1892.

[47] VIGNAL, W. "Formation et Développement des Cellules nerveuses de la Moelle des Mammifères," *Compt. Rend.*, 1884.

[48] WALLER, AUGUSTUS. "Experiments on the Section of the Glossopharyngeal and Hypoglossal Nerves, and Alterations produced in the Structure of their Primitive Fibrils," *Phil. Trans. Roy. Soc. of London*, 1850.

[49] WALLER, AUGUSTUS. "Nouvelle Méthode pour l'Etude du Système nerveux," *Compt. Rend.*, 1851; also in *Archiv. für Anat. Phys. und wiss. Med.*, 1852.

[1] The author is deeply indebted to Dr. J. H. Ashworth for having drawn his attention to this paper.

Explanation of Plates.

Abbreviations.

Basal ves. = basal vesicle of cone; *cone* = retinal cone; *ep.* = external epiblast; *vent.* = ventricular cavity of brain; *y. gl.* = yolk-globule.

All the microphotographs (except fig. 4) were taken by means of an oil immersion lens, the magnification shown in figs. 1, 2 and 13 being as much as 1,500 times.

Fig. 1.

Inner part of the wall of the cerebral vesicle of an early frog embryo. Germinal cell in mitosis. Note the scanty character of the cytoplasm, as also the assimilative poles of the neuroblast-nuclei.

Fig. 2.

A large basal vesicle of achromatic material, which is continuous with the interior of the cone-nucleus. Retina of a thirty-fifth day frog embryo.

Fig. 3.

Wall of cerebral hemisphere of tenth day frog embryo. Note the assimilative poles of the nuclei, with one of which a yolk globule is in contact.

Fig. 4.

Assimilative poles of neuroblast-nuclei in a *Zoarces* embryo. They are all directed towards the central cavity, as in fig. 3.

Fig. 5.

Wall of cerebral vesicle of fourth day chick. The young neuroblasts are lying in the myelospongium network.

Fig. 6.

The whole thickness of the neopallium of a fourteenth day chick. The neuroblasts are all of the α-type, *i.e.*, practically nuclei. Part of the ventricular cavity is seen below.

Fig. 7.

Pyramidal cell region of cerebral hemisphere of a rat embryo. The neuroblasts are, at this stage, all of the β-type—becoming γ-neuroblasts later. The upper part of the section is that directed towards the outer surface of the hemisphere.

Fig. 8.

Anterior cornu of spinal cord of a twenty-fifth day frog embryo. The nucleus below the $\times$ shows a yolk globule still in relation to its axon pole. From the same pole of the nucleus below the previous one is issuing an axon rudiment.

Fig. 9.

Anterior cornu of spinal cord of a young frog. All three types (α, β, γ) of neuroblasts can be recognised. Compare with fig. 8.

FIG. 10.

Anterior cornu of spinal cord of eighth day chick. α and β types of neuroblasts can be seen. The latter shows the gradual enclosure of the nucleus by the axon.

FIG. 11.

Anterior cornu of spinal cord of fourteenth day chick. Compare with figs. 10 and 6. The nucleus is still incompletely surrounded by the developing cytoplasm. Note the oval bipolar character of the nucleus.

FIG. 12.

Anterior cornu of spinal cord. Chicken first day after hatching. The nucleus is now spherical, and has taken up a position near the centre of the cell.

FIG. 13.

Shows a yolk globule being directly converted into chromatic material at the assimilative pole of a neuroblast nucleus. From the retina of a twelfth day toad embryo.

FIG. 14.

Spinal ganglion of a *Zoarces* embryo. Two nuclei (near the crosses) show well-marked polar accumulations of perinuclear material.

FIG. 15.

The neuroblast-nuclei in the retina of a nineteenth day frog embryo. Note a lateral tilting of the assimilative pole in two nuclei (above the ×) of the ganglionic layer.

FIG. 16.

Neuroblast-nuclei in the retina of a thirty-fifth day frog embryo. Note a marked diminution in their size when compared with fig 15. Note also that the various processes appear to pass directly from the nuclei (β-neuroblast).

FIG. 17.

Retina of a thirty-fifth day frog embryo. Note the chromatisation of the basal vesicle of the cone, and compare with fig. 2.

FIG. 18.

Retina of adult frog. Note the persistence of the β-type of neuroblast in all the layers.

FIG. 19.

Retina of adult cat. Note the persistence of the β-type of neuroblast in the internal nuclear layer. The cell elements of the ganglionic layer have now reached the γ-type.

FIG. 20.

Neuroblasts of the ganglion habenulæ of a fifteenth day frog embryo.

FIG. 21.

The ganglion habenulæ of a young frog. Note the persistence of the β-type of neuroblast, and the great diminution in the size of the nuclei compared with those of fig. 20.

FIG. 1.

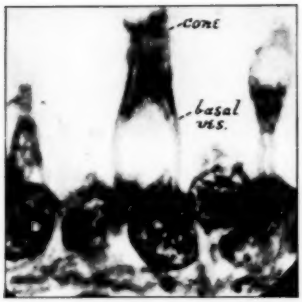

FIG. 2.

FIG. 3.

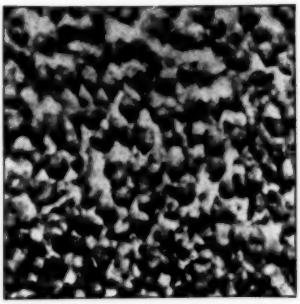

FIG. 4.

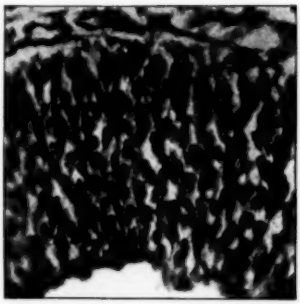

FIG. 5.

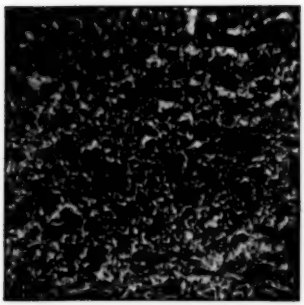

FIG. 6.

Face p. 362.

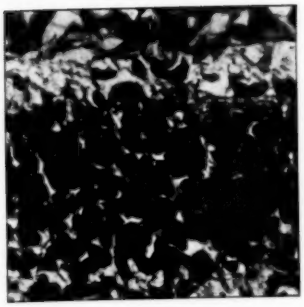

FIG. 7.

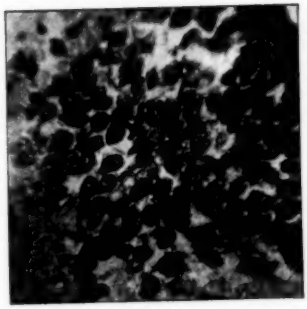

FIG. 8.

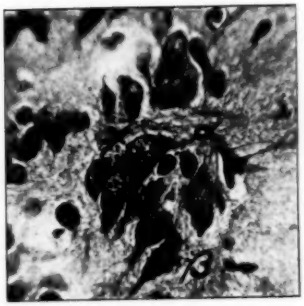

FIG. 9.

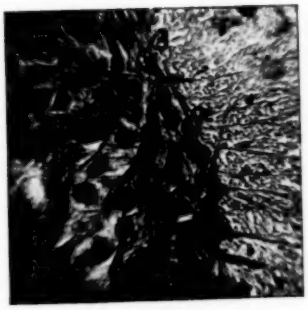

FIG. 10.

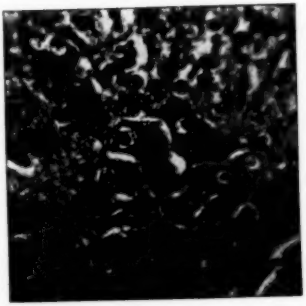

FIG. 11.

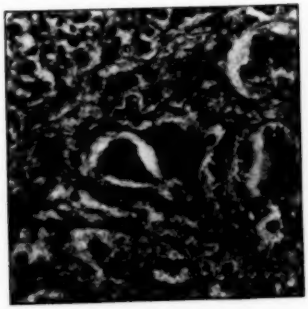

FIG. 12.

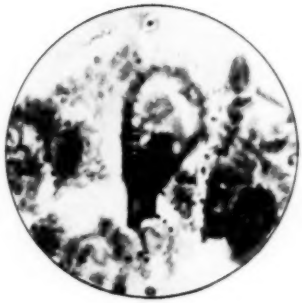

FIG. 13.

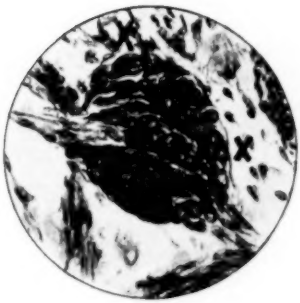

FIG. 14.

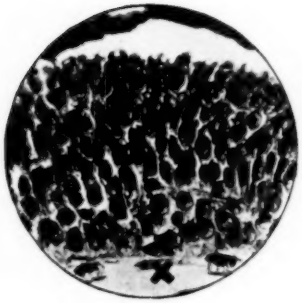

FIG. 15.

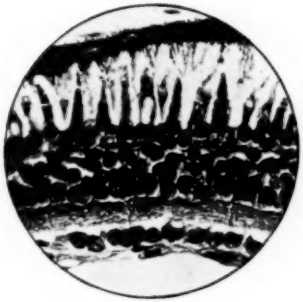

FIG. 16.

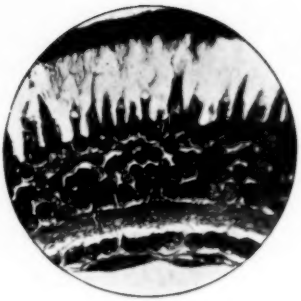

FIG. 17.

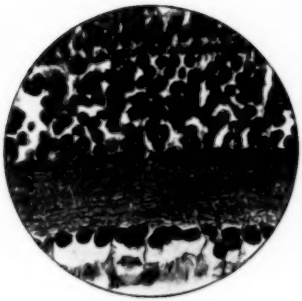

FIG. 18.

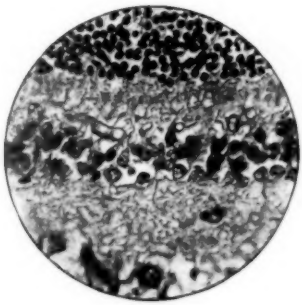

FIG. 19

FIG. 20.

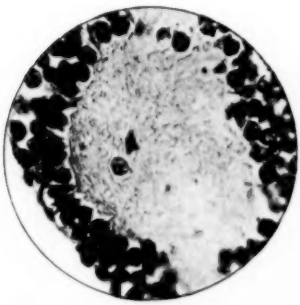

FIG. 21.

MINERS' NYSTAGMUS.

BY A. CHRISTIE REID, M.A., M.D., B.Sc.ABERD.

THE form of nystagmus known as "miners' nystagmus" has long been sufficiently known to need no detailed description here; that in Simeon Snell's admirable monograph is adequate, and a typical case is easily recognised.

It might be thought, too, that there was nothing more to be said as to its etiology. The views of Snell are generally quoted in text-books and considered adequate to the explanation of the phenomenon. He came to the conclusion that "the nystagmus of miners is a myopathy dependent on the peculiar position assumed by a certain class of men in the mine. . . . Later researches have substantiated in the fullest manner those already published. . . . Of all the many instances which have at different times come under my notice, with very few exceptions the miners have been those whose work has been done on their sides, more or less, in connection with the work called 'holing.' . . . It is, I believe, a myopathic disease, a local affection. . . . Chronic fatigue in the ocular muscles is brought about and, atony being induced, oscillation of the globes is caused."

This is the generally-adopted theory. One of the main objects of Snell's work is to discount the influence of feeble illumination in the causation of the affection, though he admits that "the worse the light the greater will be the effects of the strain experienced."

Other observers have at different times put forth views more or less at variance with these; it must be admitted, however, that no one goes the length of propounding a theory in opposition to the "myopathic theory" with anything like the thoroughness of Snell.

Jeaffreson [3] states that in his part of the Durham field little or no holing is done ; he thinks that a cramped position, such as sitting on the haunches, has much to do with the causation producing " cerebral anæmia," but " chiefly of those parts which derive their supply from the basilar arteries, *i.e.*, the occipital lobes; this is caused by pressure of the tentorial ring, when the head is thrown far back on the upper part of the pons." The cramped position, he says, leads to " a dissociation of naturally-associated centres." He proposed to change the name from " miners' nystagmus " to " miners' neurosis " because of the often associated general nervousness.

Court, senr. [1] of Staveley, Derbyshire, specially investigated the question of the comparative influence of naked lights and safety lamps (the naked light being the stronger illuminant). He examined 524 men who worked with lamps, and 573 men who worked with naked lights. He found that 161 of the 524 were afflicted with nystagmus, and, in striking contrast, only 32 of the 573 who worked with naked lights (29 of these 32 had previously used lamps).

These figures lead Court to maintain " that the insufficient light of the safety lamps is the chief, if not the sole, cause of the nystagmus, and that position has very little, if anything, to do with it." With Snell's writing in view he goes on to say : " If the cause of the nystagmus be, as Snell says, the position of the head and eyes directed obliquely upwards during the process of holing, how is it that in naked light mines, where the work of holing is done in exactly the same way as in the safety lamp pits, there is comparatively no disease at all? The statement, moreover, that the miners have their heads and eyes directed obliquely upwards during the process of holing is contrary to fact."

He [2] returned to the subject in 1892, emphasising his conclusions and producing photographs of men actually holing, which show no upward movement of the eyes. " The direction of the man's eyes while he is lying down is straight before him, and he looks at the cleft in the coal, which measures in height from about 9 to 3 inches. The

eyes are not turned obliquely upwards. What strain, I ask, can there be upon the eyeball muscles in this position?"

Further than this Court does not go, having proved that a very feeble light is a factor of prime importance, he leaves the *causa causans* to be sought for.

Tatham Thompson [12] brings forward interesting evidence of somewhat the same nature from South Wales. In the mines he refers to are two kinds of coal; (1) house coal in thin seams, worked with naked lights, by holing; (2) steam coal in thick seams, worked with feebler safety lamps, by straight work, without holing.

Nystagmus is much more common in those who work the steam coal. In summing up he says: "I would submit that . . . visual strain, with insufficient illumination, is, at any rate, as great a factor in the causation as strain of the ocular muscles."

Several attempts have been made to show that miners' nystagmus is not a disease by itself, and to classify it in our general scheme of diseases, Bell Taylor [11] places it along with other occupation neuroses, such as writer's cramp. Thus: ". . . . especially the superior recti and the inferior obliques (are involved), the fatigue necessitates a series of little successive and rapid contractions, it then produces nystagmus, or, rather, gives rise to vertical oscillations. To explain the horizontal we have recourse to the internal recti and the accommodation . . ." And, again, as late as 1887, he wrote, "miners' nystagmus appears to be a pure myopathy and strictly analogous to writer's cramp."

A. Nieden [6], whose work is the standard in Germany, speaks of the myopathic as "the only hypothesis remaining on a sure foundation," and claims that the superior rectus, inferior oblique, internal and external rectus are involved. His conclusion is that it is a fatigue tremor, analogous to that met with in the leg when in the sitting posture, the weight of the limb is thrown on the toe, or in the upper extremity on holding a weight at arm's length. He states that the superior recti are, of all the ocular muscles, least able to stand strain, because of their insertion (7·7 mm.

from the corneal margin), cross-section and volume; and the inferior obliques come next in this inability.

His view, however, is hardly identical with that of Snell. "Normally the will controls the complex nerve impulses, which stream down in succession to the muscle and cause tonus. In addition to this, on voluntary movement a stronger impulse is sent down; if tonus is lacking this voluntary impulse causes a tremor in the muscle; no continuous contraction is possible. . . . Nystagmus is due to failure of tonus. No known electrical stimulus can produce a clonic (*zitternd*) contraction in a fatigued muscle; if strong enough to cause contraction at all this contraction is continuous, therefore fatigue alone cannot cause nystagmus, failure of tonus must be postulated." Further, "Nystagmus is thus a neuropathy that affects the muscle substance only secondarily; there is really no distinct muscle affection, the muscular movements are complete in every direction, only the manner in which they are brought to rest, when put in action, is disturbed. There is no cramp, because in cramp there is an excess of nerve energy sent down, here there is a diminution."

From consideration of a goodly number of cases, I have come to the conclusion that no theory hitherto enunciated is in accord with all the facts, and it is the purpose of this paper to attempt a reconciliation between the seemingly antagonistic views of the myopathists and those who hold that feeble illumination is the main factor. The point I wish to prove is that fatigue of the muscles is not an essential etiological factor, and also that "fatigue" of the nerve centres is a somewhat misleading term, indicating that the centres have been worked too hard. I hope to show that they have not been worked enough. I maintain that the affection is due to a disturbance of the centres having to do with the equilibration of the eyeball; and the theory which I shall put forward may be styled the "Equilibration disturbance theory."

The pit at which I made most of my observations, Hickleton Main, South Yorkshire, has an eight foot seam. The position assumed by the hewer at work is not in any

sense constrained; the men never lie down to get the coal, they work straight at the coal face, standing more or less upright; no holing is done, save occasionally by a few selected men, in road making. The only one of my patients who admitted to holing in this way stated most explicitly that he did not find the position then assumed any more trying to his eyes than the upright position.

I could not therefore accept the view that fatigue of the elevators due to constrained position was the main factor in the causation of nystagmus among my patients. Another fact that made me sceptical was the rotary character of the movements even in those slight cases in which they can be elicited only on turning the eyes upward. If due to weakness of the elevators, surely one would expect a downward, succeeded by a correcting upward, twitch. What does take place is a rhythmical contraction in which probably all the other muscles of the eye take part, producing a beautiful rotatory movement. In many cases, indeed, in which the movements are evident only on gazing upwards, they are mainly from side to side, thus proving rhythmical contraction of at least the external and internal recti.

The fact that the same form of nystagmus is not always found in the two eyes seems impossible of explanation on the position-fatigue theory. Thus Nieden found in four cases pure horizontal in one eye and vertical in the other; in sixteen cases horizontal in one eye and rotary in the other. Several other considerations appear to me to point to the inadequacy of the muscle-fatigue theory. Thus, on dissociating the images of the two eyes by some such device as I used in Case 8, the onset of nystagmus, the gaze being horizontal, clearly proves, I think, that the nystagmus depends less on an inherent muscular weakness than on a defective central coördination (*vide infra*).

Another point against the myopathic theory is, I think, the fact that nystagmus may occur in positions other than those of the upward gaze. In many cases even on looking downward the nystagmus continues, and in one or two of my cases it was most marked on looking to one side, *i.e.*,

using only the external and internal recti. If in these cases fatigue is the prime causal factor, then a general fatigue of the six or seven muscles must be postulated, and how position of the body, be it ever so fantastic, can bring this about, I quite fail to see.

A further question I would ask the myopathists is: Have they ever demonstrated fatigue of the elevators? *i.e.*, can they bring evidence to prove that the eyes are incapable of such an extensive upward movement as those of a normal individual? Nieden states the contrary. Hughlings Jackson [6], moreover, speaks of the "complete excursions of the globes." It occurred to me that evidence of fatigue might be sought for by testing for hyperphoria with Maddox' rod. I found that in most cases there is absolutely no hyperphoria; thus, of eighteen cases tested, ten showed no hyperphoria but slight esophoria; four showed absolute orthophoria; one showed no hyperphoria, but considerable exophoria; one showed no hyperphoria, but slight exophoria; two showed slight hyperphoria with considerable esophoria. I think I have now brought forward enough evidence to throw considerable doubt on the adequacy of the muscle-fatigue theory. We must search for a deeper cause.

Physiologists tell us that fixation of the eye is mainly a reflex, dependent chiefly on the higher visual acuity of the fovea, and particularly of the macula [8], "with dark adaptation, however, visual acuity is equally good in all parts of the retina, except in the fovea, where it is lowered."

Darkness, then, does away with the possibility of superior macular images. Here, surely, is a factor of the first import in causing a tendency to instability of the globes, and such occurs whenever we shut our eyes. Let us go a step further. It is a well-known fact that the equilibration of the eyes is very closely related with the equilibration of the body; this is demonstrated by two converses: (1) The equilibration of the body is controlled to a great extent, by afferent impulses from the eyes, and for this reason Romberg's test in tabes is performed with the eyes shut; (2) when the equilibration of the body is disturbed that of the

eyes is apt to be disturbed also, and not in a haphazard way. I may cite in this connection the experiments of Cyon and Lee on the semicircular canals of fishes which established not only the equilibrating function of these canals but also the remarkable connection between them and the equilibration of the globes.

I cannot but think that the underlying common causal factor in all kinds of nystagmus is a disturbance of the centres whose normal action is to maintain the equilibrium of the globes in whatever position they are placed. One cannot be more precise; the term "equilibration centres" saves a cumbrous periphrasis.

Can we then postulate factors in the miner's life sufficient to derange the function of these centres? I think we can. (*a*) The imperfect fixation due to dim light; (*b*) a constant tendency while at work to disturb the equilibrium of the body, as when he lies on his side, sits on his haunches, balances himself on the top of a tub, or stumbles about among the hewn lumps in his thick clogs, often much worn down at the sides.

I have proved, however, that even in daylight a disturbance of the equilibrium of the body is of itself sufficient to make manifest a latent nystagmus.

Thus, if a miner with latent nystagmus is asked to turn round as quickly as possible, with his eyes shut, several times in succession, around a vertical axis, till slight giddiness results, and is then asked to fix any object near or distant, above, below, or on a level with his eyes, the nystagmus will be rendered evident when other means, such as making him look upwards, have failed to elicit it. I performed this test on many occasions with uniform success; it may be briefly referred to as "the rotation test." A true rotary nystagmus may be thus elicited: if rotary it is obviously not merely compensatory, as in the turn-table experiments. It is a very delicate test. In one man, who had been off work for two years with a fracture, I was able by this means to elicit a well-marked nystagmus, which could not be elicited by making him look upwards. Surely the myopathists could not claim this case as one of "fatigue of the elevators" after two years of complete rest?

A similar experiment is to ask a man with latent nystagmus to "toe a line," walking heel to toe for a few yards with eyes shut and without support, then asking him to open his eyes and fix a spot on the wall some 6 m. distant, on a level with his eyes; the nystagmus may then be quite evident.

Neither of these tests puts any strain on the elevators; they tend, however, to disturb the bodily equilibrium.

But ocular instability is not rotary nystagmus. Why is there almost always such beautiful rhythmic rotation about a sagittal axis? Is there anything in the miner's work which would tend to cause regular rotary movements of the eyes in unison? Surely there is. Whatever position he assumes in getting the coal he performs a series of regular rhythmical movements with his pick, swinging from either shoulder, his head revolving in consonance with these movements. The regularity and rhythm of these movements is very striking to any one who has seen him at work.

At the same time his eyes are more or less fixed on the piece of coal he is hewing. I say more or less because I am not at all sure to what extent nystagmus, occurring while at work, is compatible with vision sufficiently accurate for the precise hitting of the point aimed at. I have been told more than once by a miner down below, who had just ceased hewing, that his eyes were steady, whereas they were in violent nystagmus.

There is a tendency for the eyes to perform compensatory movements in the dark as in the light, and the miner's, no doubt, rotate in precisely a similar way as does his head. Fixation in the dark is, as we have seen, very difficult, because the fovea cannot be used; hence the movements tend to escape from control, and the habit unconsciously acquired down below at work persists when he leaves it.

I had already arrived at these results before I came across Jeaffreson's lecture [3], which I think amply confirms my main contention; after all there is not much difference between "dissociation of centres normally associated" and my "equilibration disturbance" theory. I think the introduction of the conception of equilibration

carries us a step further. I cannot, however, agree with his theory of cerebral anæmia, nor with Mr. O. Oglesby's theory of "venous engorgement of the medulla." [7].

I think we can also agree with Jeaffreson that "in all cases the condition of the refraction and accommodative power should be enquired into, as it certainly plays some secondary part in the feelings of distress from which the patient suffers." Correcting glasses will certainly tend to more distinct vision and greater activity of the macular region, hence to firmer fixation; and on this theory it is quite easy to understand that "in some cases the relief is magical."

Hermann Wilbrand [13] seems to have come very near the conception of equilibration disturbance when writing on the theory of nystagmus in general. Nieden ridicules Wilbrand's theory, but I am convinced, from a closer examination of his writing, that he comes nearer the true solution than has been generally supposed; for he finds an analogy between nystagmic movements and the efforts of the body to maintain the body equilibrium. Thus he says: "As the contraction of any muscle in the body disturbs the bodily equilibrium and stimulates the centres to an antagonistic movement; so with the eye." But in speaking of miners' nystagmus he follows the rest in regarding it as having an etiology of its own, speaking of "a paresis of the elevators and a concentric contraction of the visual field," which have not been proven. On this subject, however, it is clear that he speaks from second-hand information.

To what extent this theory of the etiology of miners' nystagmus may throw light on other forms of nystagmus I am not yet prepared to say; but I think it may be applied with advantage to such cases as Snell has more recently brought forward of "Nystagmus in occupations other than mining." Space does not permit of a criticism of these cases here.

Snell's main argument for fatigue of the elevators is based on the fact that in very many cases of latent nystagmus it may be at once elicited on directing the gaze upward.

This need prove no stumbling-block; the upward gaze—without a corresponding upward movement of the face—is a most unnatural one; it is with great difficulty that we fix and accommodate in looking upwards; in fact, in the upward gaze, when looking at infinity, there is a tendency to divergence (Maddox [5]).

So Suter: [10] "The greater degrees of convergence are usually associated with downward rotation of the eyes, as in reading. On this account convergence for a near object is accomplished with much less fatigue when the object is below than when it is above the eyes." In the language of the equilibration disturbance theory, fixation in the upward gaze transmits a weak impulse to the centres, and if from any other cause these centres are disorganised the tendency to ocular instability becomes manifest.

It is a well-known fact that if the equilibrium of the body is dependent on afferent impulses from the eyes to a greater degree than usual, the balance may be disturbed by directing the gaze to the ceiling. Thus in tabes; in certain cases Romberg's test may be positive without shutting the eyes by merely asking the patient to look at the ceiling. It may be objected, as Snell asserts, that in some cases the nystagmus is most marked in the oblique upward glance, corresponding to the side on which the holer lies; for instance, a man who habitually lies on his right side may manifest nystagmus most easily on looking upwards to the left. To this I would say that because in this constrained position he has become accustomed to trust to the extra-ocular afferent impulses for the maintenance of his bodily equilibrium, it is in this position of the eyes that dissociation between the body and the eye-equilibrating centres occurs, and such dissociation may lead, as we have seen, to nystagmus.

The detailed notes of thirty cases would be tedious reading. A few points, however, bearing on the matter under discussion may be mentioned.

Case 3.—S. C., aged 35 years, a hard drinker at times, worked eleven years in this pit; dates nystagmus from six months; this is well-marked especially on looking up, violent rotary. Six

months after I first saw him I had him in bed with a fractured tibia; after a fortnight's rest the eye movements were as bad as ever, worse at twilight, and, when the lamp is first lit in the room. Even when lying quiet, it seems to dance up and down, but later on, as he gets accustomed to the lamplight, the eyes become steady. He can steady his eyes by looking strongly upward or to either side, and has often resorted to this device when down in the pit.

Ths case is interesting as showing clearly the influence of a feeble light in causing the movements, and of dark adaptation in checking them. Also it seems to tell against the fatigue theory, because when the muscles are strained the movements may become less.

Case 4.—J. B., aged 37 years, illustrates the same points. After a two months' rest from pit work his eyes became much steadier. The rotary movement is, however, easily elicited for a short time by asking him to stoop, swing about his arms, as if working with a spade, keeping his eyes all the time fixed on the floor, and then suddenly assuming the erect posture and looking straight forwards or upwards. But even in this upward position a sustained effort steadies them, and he is conscious of the moment when they become steady. How could a sustained effort suddenly steady a fatigued muscle?

Case 6.—T. A., aged 36 years, is typical in some respects, but peculiar in this that the nystagmus is most marked on looking straight forwards at a bright light on a level with his eyes, somewhat less on looking up and away from the light, or to either side, or on convergence.

Case 8.—M. F., aged 34 years, illustrates the same point, viz., "eyes steady when looking at me. On extreme vertical movement a fine nystagmus is elicited which becomes much more marked on looking to extreme right or left (horizontal), well marked also in all positions below the horizontal."

Another point to which I referred above is brought out by this case, viz., that the nystagmus may be made manifest merely by dissociating the images of the two eyes. When the cone-muscle test of Mr. Davidson was used, after getting the ring and flame correctly centred at 10 feet, a violent nystagmus, which had not before been evident, ensued, preventing further accurate observation.

This proves, I feel sure, that the nystagmus depends on a defective central coördination, because when either one well-defined impulse is sent to the brain, or when two are sent such that the desire for fusion is easily gratified the centres are not, as it were, put out of their reckoning. But if two distinct images, such as a candle flame and a ring of light, send impulses to the brain so as to compel simultaneous vision without the possibility of fusion, the centres are, as it were, taken by surprise, and are unable to control the equilibrium of the eye. In this connection the paper by Emil Levi, [4] of Stuttgart, is of interest, in which (a boy, aged 10 years) a horizontal nystagmus ensued whenever either eye was occluded as with the hand or a flat metal disc.

Case 15.—C. B., aged 35 years, has been alluded to; he had been off work nearly two years with a fracture. Says he sometimes noticed the lamps dancing when down the pit, but cannot describe any exact direction; he worked at the coal face here. No nystagmus was evident on upward gaze, and no symptoms were present; but on rotation with eyes shut "a well-marked nystagmus ensues on looking at the electric filament held at a level with his eyes. When trying to fix the light the eyes wander from fixation in the direction of rotation, then jerk quickly backwards by a seeming voluntary effort, this to and fro movement being repeated with diminishing amplitude several times, constitutes the nystagmus; the rate is about 100 per minute, it is much more easily elicited, and much more marked than it might be in a normal individual, two or three turns sufficing." It seems to indicate that control over the compensatory movements is still somewhat lacking, even after a fairly long interval.

Case 17.—A. A., aged 34 years, illustrates several points above referred to. Symptoms present for five years; although he worked here for ten years he has done only eleven months holing in his life, and during that time had no symptoms. Some time ago his eyes got so bad (nystagmus) that he had to work on the top for two years, again he tried down below, and in seven or eight months was as bad as ever; he does stone work now, and though this requires frequent up-glancing at the roof, he says it is not more trying to the eyes than ordinary work at the coal face.

Seen December 29, 1904, at 5 p.m., while recovering from

influenza; after the fatigue of walking to the surgery the eyes showed a violent nystagmus, even below the horizontal, which subsided after half an hour's rest. But on asking him to shake his head from side to side it became as bad as ever, so that he could not discern the figures on Maddox's tangent scale at 5 m. when looking straight; on suggesting to him to turn his eyes strongly to the left, he could then read them while holding the head somewhat turned in the same direction.

The movements seem to be more or less circular, complete and in + direction (hands of watch); he says—and this is the general experience—that the movements are always worse at dusk, better in daylight or the dark.

Case 19.—J. S., aged 45 years, is a man who worked eighteen years in a neighbouring pit where holing is done; he had no symptoms then. Has been here two years, and during this time symptoms have gradually come on, always worse at dusk.

On examination, blinking was very frequent (photophobia), the rotary movement was violent, most marked on directing gaze upwards, but also slightly below horizontal.

On rotation of the body, as above described, the movement became even more violent, and this even on looking down.

After a few days' treatment the eyes were steady, save on upward gaze; on rotation of the body the movement was easily elicited below the horizontal; on toeing a line, which he does only fairly, marked rotary nystagmus is induced, even with gaze downwards. No hyperphoria at 5 m. or 1 m.

Case 22.—S. B., aged 65 years, here eight years, no symptoms (or very slight on close questioning); previous fifteen years at Houghton Main, all holing, no symptoms; previous to that, twenty-two years at Rotherham, no holing: there symptoms began somewhat suddenly while working with very poor lights, noticed eyes bad one early morning in the dusk while going to work; the lamps danced, never up and down, always from side to side, not in circles.

On upward gaze a very fine rotary nystagmus is noted; he is aware the moment it comes on, but says the objects looked at do not move. The movement is much more marked on looking to either side, mainly horizontal with some rotation, amplitude greater.

A week later he came to surgery after a longish walk, and the movements were much more marked at the beginning of the examination, *i.e.*, before he had rested. A fine rapid nystagmus

is noted (with reflected light), even on looking at the floor, and the character of the movement does not at all change on slowly elevating the eyes, save that in extreme elevation the amplitude of movement is much less. A violent movement ensues, with much greater amplitude, on trying to fix a light on a level with eyes, about 2 ft. away. While sitting looking at the wall about 8 ft. away a horizontal nystagmus suddenly begins, which cannot be checked by blinking forcibly (as is sometimes the case). After half an hour's rest the eyes are much steadier, and the test of toeing the line gives no nystagmus below the horizontal. On rotation, only a temporary nystagmus, mainly from side to side. No hyperphoria.

Case 23.—E. H., aged 42 years, has never done holing nor worked in constrained positions; says two-thirds of his work is on the floor; sometimes the lamps dance; he can sometimes produce the movements by shaking the head from side to side. Movements noted only on upward gaze, most marked in right oblique position: at first a mere jerking to recover lost position, then a quite different rotary movement begins.

Case 28.—S. T., aged 31 years. Here five months. Has worked on the coal face ten years. No holing last four years; before that did a good deal without symptoms; only occasional "dancing" till six weeks ago, since then more severe; the lamps go "from side to side and round about."

Rotary nystagmus well marked on the slightest movement of the eyes above the horizontal, and in the primary position at once on shaking the head from side to side.

The next day, sitting in a chair looking straight forward, the eyes are steady. A slight shake of the head from side to side at once induces nystagmus, even on looking down, which does not cease for some time, but can be stopped at once by blinking rapidly. This was very striking, and I confirmed it several times to make sure that no other movements were being made.

When the eyes were steady, after a rest, hyperphoria was tested for, but was absent. On toeing a line marked rotary nystagmus was elicited, even below the horizontal, which subsided on blinking.

Conclusions.

The etiology of miners' nystagmus is complex. Several factors are of importance:—

(1) Conditions tending to do away with yellow spot fixation, *e.g.*, feeble light.

(2) Conditions tending to disturb the equilibrium of the body.

(3) Conditions in which some more or less rhythmical series of movements is performed by the body and head, the eyes remaining fixed.

(4) The onset is hastened by debilitating influences, *e.g.*, alcoholism, influenza, accident.

References.

[1] Court, Senr. Pamphlet now out of print, published by the Derbyshire Miners' Union, 1891.

[2] Court, Senr. "Report of Ophth. Section of Brit. Med. Assoc." *Brit. Med. Jour.*, 1892, vol. ii., p. 836.

[3] Jeaffreson. "Abstract of a Clinical Lecture on Miners' Nystagmus." *Brit. Med. Journ.*, 1887, vol. ii., p. 109.

[4] Levi, Emil. "Ein Fall von Nystagmus bei monocularem Sehen." *Mitth. aus d. Charlottenheilanstalt f. Augenkranke in Stuttgart*, 1901. Tübingen.

[5] Maddox. "The Ocular Muscles." Bristol, 1898.

[6] Nieden. "Der Nystagmus der Bergleute." Wiesbaden. 1894.

[7] Oglesby. "Nystagmus." *Brain*, 1880, vol. iii., p. 177.

[8] Schäfer. "Text-book of Physiology," vol. ii., 1900.

[9] Snell, Simeon. "Miners' Nystagmus." Bristol.

[10] Suter. "Refraction and Motility of the Eye." 1904. New York. Appleton.

[11] Taylor, Bell. "Observations on Miners' Nystagmus." *Lancet*, 1875, vol. i., p. 821.

[12] Thompson, Tatham. "Affections of the Muscular and Nervous Systems." *Trans. Ophth. Soc.*, 1891, vol. xi., p. 87.

[13] Wilbrand, Hermann. "Ueber den Nystagmus." *Sonderabdrücke der deutsch. Med. Zeitung*, 1884, Hft. 36.

Reviews.

Removal of the Gasserian Ganglion.

The Surgical Treatment of Facial Neuralgia. By J. Hutchinson, Junr., F.R.C.S. London, 1905, John Bale, Sons & Danielsson, Ltd.

The Sensory Distribution of the Fifth Cranial Nerve. By Harvey Cushing, M.D. *The Johns Hopkins Hospital Bulletin*, July-August, 1904, vol. xv., Nos. 160-161.

The Surgical Aspects of Major Neuralgia of the Trigeminal Nerve, February, 1904. Reprinted from the *Journal of the American Medical Association*, March 11, 18, 22, and April 1 and 8, 1905. Chicago: Press of the American Medical Association.

Sixteen years have elapsed since the Gasserian ganglion was first removed for the cure of trigeminal neuralgia. On April 2, 1891, Rose removed the ganglion by the pterygoid route. Eight months later the first operation by the temporal route was performed; Sir Victor Horsley avulsed the roots of the fifth nerve intradurally. These two operations mark the commencement of the radical surgical treatment of epileptiform neuralgia.

Nearly two years later [1892], Hartley and Krause independently devised an operation through the temporal region, reaching the ganglion by stripping the dura mater from the middle fossa of the skull. Many modifications of these two early methods of approach have been proposed, the effect being, as Cushing has pointed out, "to make the low operation higher and the higher lower, a tendency, in other words, towards a more direct or trans-zygomatic route."

The approach devised by Cushing is the best of these modifications. He makes a skin muscle flap in the temporal region, removes the zygoma and opens the skull in the lower part of the

temporal fossa. In the development of this method of approach, the aim has been to obtain as direct access as possible to the ganglion, leaving little permanent deformity. In making the skin flap, Cushing pointed out that the anterior limb should not extend below the external angular process of the frontal bone. Lately he has modified the skin incision still further, so as to avoid injury to the branches of the facial nerve supplying the frontal portion of the occipito-frontalis.

The opening in the skull is below the middle meningeal artery, and it is possible in most cases to complete the operation without injury to the artery. Cushing was able to do this in nineteen out of twenty cases, and Dollinger has shown it to be possible in 94 per cent. of skulls. This method of approach differs from all others in being, as he has termed it, direct temporal and infra-arterial. A somewhat similar operation is practised by Lexer.

Of those operations evolved from the pterygoid route, one only, Juvara's, resembles the low temporal operation, but it remains, as Cushing points out, too low. "The extra cranial dissection is carried unnecessarily far . . . namely, to the second and third divisions at their emergence from the skull, the floor of the temporal fossa alone having been removed." Both Poirier's and Doyen's operations differ from Cushing's. Doyen resects the zygoma and coronary process of the inferior maxilla, ligates the internal maxillary artery and rongeurs away the base of the skull as far as the ganglion, it is begun as a high temporal operation and finishes as a low pterygoid. Poirier uses a similarly complicated method of approach. I am unable, therefore, to agree with Mr. Hutchinson that "In all essentials what has been described as Cushing's method is identical with M. Poirier's procedure."

Mr. Hutchinson mentions that it is strange that Mr. Cushing and Professor Kocher (who writes of the former's modification as original, and constituting a great improvement) do not mention Poirier's work. But Mr. Hutchinson has overlooked the fact that in Cushing's paper to which he alludes, it is expressly mentioned by name. As Cushing has himself written of his own method "the operation differed only in detail from others previously described, but that in the observance of detail hung the success of delicate surgical procedures of this sort."

At the present time practically all surgeons in this country and America and many of those on the Continent approach the ganglion by the temporal route, the majority by the high temporal (original Hartley-Krause) operation. Those who have

operated and obtained good results by this approach will be unlikely to change their method; but as far as ease of exposure is concerned, the operation devised by Cushing and Lexer is the best and is the approach which should be used by those not skilled in the high operation.

Briefly, its advantages are these. The approach is more direct, hence the degree of compression of the temporal lobe is less, the mortality lowered, shock lessened, and the complications of aphasia and hemiplegia, temporary or permanent, avoided. The middle meningeal artery is avoided. The deformity remaining after removal of the zygoma is less than when this bone is left in position, and by the incision employed it is possible to inflict little or no damage to the branches of the facial supplying the muscles of the forehead.

There is one other point that needs mention; the best method of opening the skull. Many ingenious saws and osteotomes, some worked by hand, others by motors, have been used. The simplest method is, as so often happens, the best. Sir Victor Horsley, in the address on surgery at the meeting of the British Medical Association this year, said: "The bone should be divided with as little vertically applied force as possible, and removed with the least possible pressure on the brain and dura mater. After a long experience of saws, circular or straight, and trephines driven by electro-motors, I find that the foregoing principle can be most quickly and readily fulfilled by first removing a trephine disc. . . . and finally cutting away the bone with bone forceps."

In this operation it is never necessary to replace any of the bone removed.

The aim of all intracranial operations carried out upon the fifth nerve is completely and permanently to abolish sensory impulses passing upwards from the territory it supplies.

The first operations performed for this purpose were removal of ganglion (Rose) and avulsion of roots (Horsley). The procedure carried out the greatest number of times is undoubtedly removal of the whole ganglion together with its roots. This is the procedure adopted by Horsley, Krause, Cushing and Lexer, among others. When successfully carried out and the ganglion definitely removed, a cure is assured; relapses do not occur.

Ferrier, Spiller, Barker, among others, have suggested section of the sensory root in place of removal of the ganglion; this has been carried out with success by Frazier and by Sherman. The advantage over removal of the ganglion lies in the fact that in some cases it is possible to spare the motor root, and even if it

be necessary to divide it, regeneration would almost certainly occur. But clinical as well as experimental evidence is conflicting as to the possibility of the regeneration of the posterior roots after section; until this is settled we shall be doing the best for our patients in choosing an operation known to be curative. That removal of the whole ganglion can be placed in this category is no longer open to doubt, and of late, surgeons have been endeavouring to develop less severe operative procedures upon the ganglion itself and upon its primary divisions in their intracranial course. The name of Mr. Hutchinson is associated with this work. In cases in which the neuralgia does not affect the territory supplied by the first division he advocates removal of the intracranial portions of the second and third divisions of the nerve together with the corresponding portion of the ganglion, leaving the roots and the first division intact. The reasons which he brings forward in support of his views are weighty. He points out that the first division is rarely affected, even in severe and neglected cases. With regard to the operation itself, shock is less, for it is during the elevation of the temporal lobe that shock is most marked, as the blood-pressure charts of Cushing show. This elevation is greatest in the operation of complete removal at the time when the first division is being freed; it is at this time also that the ocular nerves coursing in the outer wall of the cavernous sinus, and even the sinus itself, is liable to injury.

Lastly, the cornea remains sensitive and the eye consequently is not endangered.

The question of the absolute curative value of this partial excision of the ganglion has yet to be finally settled. Two of Mr. Hutchinson's cases have had no recurrence seven and seven and a half years after the operation, so that I think we may fairly say that the operation is curative.

Other surgeons have recommended that the operation be confined to the second and third divisions of the nerve. Abbé, and more recently Frazier, have advocated intracranial section of these divisions, with the interposition of rubber tissue to prevent reunion and regeneration. It is as yet too early to say what will be the ultimate result of such operations, but instances have been recorded in which recurrence of pain had taken place after neurectomy without regeneration of the nerve. For this reason it is in these cases best to deal with the ganglion as well as with its divisions.

The question now arises as to the course to pursue when one

division only is affected. Mr. Hutchinson recommends that operative interference should be limited to the division affected. When the area supplied by the third division is alone the seat of pain, the root and the corresponding part of the ganglion may be removed, providing the case is early, or if the disease has been in existence for some time and shows no sign of spreading into the territory supplied by the second. When the second division is involved alone it is impossible to do this. Mr. Hutchinson records a case in which he resected a portion of the trunk of this division intracranially. No recurrence had taken place eighteen months later. But in this operation there are two possible sources of recurrence, a failure to eradicate the disease, and possible reunion and regeneration. If the operation is performed, Abbé's method of interposing an impermeable foreign body between the two ends should be made use of.

At the present time we feel inclined to agree with Mr. Hutchinson that when possible the first division may be spared. But, in consequence of the impossibility of separating that part of the ganglion connected with the third division from that of the second division, we believe it is unwise to attempt to deal with these divisions separately. Not to deal with the ganglion, but to divide the main branches only intracranially is to run a grave risk of recurrence.

The death rate of operations upon the Gasserian ganglion can no longer be spoken of in Chipault's words as enormous. It has steadily diminished from Tiffany's 100 collected cases with a death rate of twenty-two to those of Sir Victory Horsley, 120 cases with six deaths. The death rate in the cases of Cushing, Hutchinson and Lexer, is less than 5 per cent.

Sherrington first pointed out that the distribution of the three branches of the trigeminal resembled that of peripheral nerves, and not of posterior roots. But as soon as the Gasserian ganglion has been removed the lesion becomes one comparable to those of the posterior roots investigated by Sherren and Head. As on the arm, so here on the face the extent of the loss of sensibility to painful cutaneous stimuli exceeds that of the loss to deep touch. This is well demonstrated by the wonderful series of cases reported by Cushing. He alone has attempted seriously to investigate the loss of sensation, in all its forms, which follows excision of the ganglion. He examined sensibility to touch with a hair set in a handle; as thermic tests he used hot and cold tubes, or a brush moistened with ether for cold, the head of a pin warmed for heat. Unfortunately, as the writer has found,

the space between the two borders of loss of sensation is usually small, and the hairs of the cheek frequently spoil the field for investigation; this makes it difficult to apply truly differential tests. But it is greatly to be hoped that Cushing will continue his admirable observations on the large material at his disposal, paying particular attention to the nature of the sensibility existing within the zone of dissociated loss of sensation.

JAMES SHERREN.

Untersuchungen über den vom Vestibular-apparat des Ohres reflektorisch ausgelösten rhythmischen Nystagmus und seine Begleit-erscheinungen. (Ein Beitrag zur Physiologie und Pathologie des Bogengangapparates.) Von Dr. Robert Bárány. Pp. 107. Berlin: Oscar Coblenz, 1906.

IN a recent paper on the Physiology and Pathology of the Semicircular Canals, Dr. Robert Bárány, Assistant in the University Clinic for Diseases of the Ear, Vienna, publishes the results of researches, which are of considerable interest from the practical standpoint. As an outcome of these researches Dr. Bárány recommends and employs certain methods of examination, with which the writer, on a recent visit to Vienna, had some opportunity of becoming acquainted, and which he thinks are worthy of a fuller recognition in this country than they have hitherto received.

Although it is probable that the vestibular organ is of less physiological importance in man than in many animals (notably birds), it is well known that its stimulation in health gives rise to certain well-marked effects of both a subjective and an objective nature, and that in diseased conditions these effects undergo important modifications. Among the methods of stimulation may be mentioned active and passive turning of the body round a vertical axis with the head in different positions, and alterations of temperature by means of syringing with hot and cold water; but these, with others, will be referred to in more detail later. In the first place the following effects of stimulation will be considered.

(*a*) *Nystagmus.*—Two distinct forms of nystagmus may be observed under different physiological and pathological conditions, of which one is known as undulatory, and the other as rythmical nystagmus. The second is the form which is associated with stimulation of the vestibular organ. Vestibular nystagmus consists of a slow and a fast movement, the difference

between which is usually quite clear. It is usual to consider the direction of the nystagmus as indicated by the direction of the fast movement, and, in rotatory nystagmus, by the direction taken by the upper end of the vertical iris meridian in executing the fast movement. The nystagmus, when very intense, may be observed with the eye in any position, but it is always best marked when the gaze is turned in the direction of the fast movement, and becomes much weaker or disappears entirely when the eyes look straight forward, or are directed to the opposite side. As to the cause of the nystagmus, the conclusions of Mach and Breuer are to-day almost generally accepted. A movement of the endolymph in one or more of the semi-circular canals, brought about by a change in the position of the head or by other means, causes a displacement of the cupula of the crista ampullæ, the result of which is an impulse along the vestibular nerve, which reflexly gives rise to nystagmus. So long as this displacement continues the nystagmus will continue, but since the elasticity of the ampullary hairs tends to replace the cupula the nystagmus may cease even while the turning movement of the head is still continued. As a matter of experience the nystagmus usually ceases after from four to six complete revolutions. Further, after cessation of the head movement, a flow of endolymph takes place in the opposite direction, which also gives rise to nystagmus. Ewald's experiments on pigeons have shown that the direction of the nystagmus depends upon (1) the choice of the canal stimulated, and (2) the direction of the movement of the endolymph. The result of these experiments has been to show that nystagmus during turning takes place in each eye in a plane of the bulb placed at right angles to the axis round which the head is turned; and that the slow movement of the nystagmus is in a direction opposite to that of the turning. For example, a right horizontal nystagmus (fast movement to the right, and slow to the left) occurs on turning to the right with the head upright; a left rotatory nystagmus occurs on turning to the left with the head bent forwards at an angle of 90°. The movement of the endolymph, which takes place when the head comes to rest, having, as has been said, a direction opposite to that of the original current, will give rise to a nystagmus, whose direction also is opposite to that of the original nystagmus. Thus, *after* turning to the right with the head erect, a left horizontal nystagmus will be observed. Spontaneous nystagmus of vestibular origin, observed in pathological conditions, is usually a combination of horizontal with rotatory nystagmus, and in cases

of unilateral disease of the labyrinth is directed towards the sound side.

(*b*) *Apparent movements of the surrounding objects.*—This visual sensation occurs under the following three conditions: (1) Voluntary eye movements, which do not attain their object (as in paralysis of eye muscles); (2) voluntary squint; (3) involuntary eye movements. Vestibular nystagmus belongs to the third of these groups, and that it is responsible for the visual sensation may be concluded from the fact that if the nystagmus be inhibited, as it often can be by turning the eyes in a direction opposite to that of the fast movement, then the apparent movements of objects in the field of vision will also cease. It must be noted that this visual sensation is associated with the nystagmus which occurs *after* turning, and not with that which is present *during* the turning. The probable explanation of this fact is that the slow movement of the nystagmus, during which the main visual impression takes place, is of such a nature and direction as to counteract the apparent movement of objects across the field of vision; the eye follows the objects as they pass in front of it, so that the latter appear to remain at rest. That this is the true explanation is supported by the observation that the apparent movements may be perceived, even *during* the turning, provided that the nystagmus has ceased, and also, as in Mach's experiment, by placing the subject in a room which is turned with him, when it is found that, the nystagmus remaining uncompensated, the apparent movements are perceived. The nature of the apparent movements varies somewhat. In some persons a visual impression occurs only during the slow movement of the nystagmus, in which case objects appear to move in a direction opposite to that of the slow movement. In others, a visual impression occurs during both movements, with the result that objects seem to move to and fro in both directions.

(*c*) *Sensation of continued rotation of the body.*—This feeling is perceived only while the nystagmus, after turning, is still strongly marked. It shows many variations in different cases. Some persons do not perceive it at all, others only with closed eyes; in others again it is easily appreciable, even with the eyes open, and the feeling is one of rotation in a direction the same as that of the apparent movement of surrounding objects. It should be noted that the direction of both of these is altered, when the position of the head is changed. Dr. Bárány was the first to observe that with closed eyes inhibition of the nystagmus, by turning the eyes in the direction of its slow movement,

causes inhibition of the sensation of rotation, and he concludes that the sensation is therefore dependent on the presence of the nystagmus, and mentions two cases of labyrinth disease in illustration. In both of these there appeared, on looking in a certain direction, marked spontaneous nystagmus accompanied by a feeling of rotation, while, when the eyes were turned in the opposite direction, both the nystagmus and the sensation ceased.

(*d*) *Reaction movements and disturbance of balance.*—As a result of stimulation of the vestibular apparatus, and at least partly related to the nystagmus, the subject, after turning, tends to execute certain movements when placed in the erect posture. These movements are best marked with the eyes closed, and cease considerably before the disappearance of the nystagmus. As is the case with the apparent movements of objects and the sensation of rotation, the reaction movements depend for their nature upon (1) the variety of the nystagmus, and (2) the position of the head. They take place always in the direction of the slow movement of the nystagmus, and in a plane passing through one or both eyes at right angles to the axis round which the head was originally turned. As might be expected, disturbance of balance occurs only when the plane of the nystagmus makes an angle with the horizontal plane. Alteration of the position of the head changes the direction of the reaction movement in a typical manner. That inhibition of the reaction movements, as a rule, occurs on inhibiting the nystagmus, by turning the eyes in the direction of its slow movement, seems probable, but in some cases this inhibitory effect appears to be slight or altogether absent.

In addition to the effects of stimulation of the vestibular apparatus already mentioned, there are others, such as clouding of the visual field and general dulling of sensation, nausea, vomiting, &c. All these subjective sensations and objective symptoms together represent the condition known as vertigo. From the point of view of the diagnosis of vertigo in pathological states the observation of nystagmus is of by far the greatest importance. Complaints by the patient of loss of balance or subjective sensations, such as feeling of rotation, &c., can only be regarded as supplying ground for the suspicion that the attacks are accompanied by nystagmus.

The methods of examination will now be considered; they are the following: (*a*) Active and passive turning round a vertical axis with the head in different positions. (*b*) Syringing with hot

and cold water. (*c*) Galvanisation of the head. (*d*) Alteration of the air-pressure in the external auditory meatus, and direct pressure on the stapes or a labyrinth fistula.

(*a*) For the examination by turning a revolving chair is employed, to the back of which is fixed a vertical bar to act as a handle. When for physiological purposes it is desired to evoke a strong nystagmus with marked subjective sensations and reaction movements, the person under examination should be turned through about six to ten complete revolutions. In cases, however, of suspected labyrinth disease of one side, it is necessary that only about three turns should be made. The reason for this is as follows: The labyrinth of each side is capable of producing nystagmus in both directions, but each labyrinth has more influence in producing nystagmus towards its own side than towards the opposite one. Hence, it follows that while, in cases of one-sided labyrinth destruction, nystagmus to either side can be produced by turning in a corresponding direction, the result of the examination will depend upon the relative intensity of the nystagmus elicited in each instance; but many revolutions produce so intense a nystagmus that this distinction is lost; hence, the necessity for turning only a few (usually three) times. Since the nystagmus, *during* turning, is directed to the side towards which the turning is taking place, and the nystagmus, *after* turning, is directed to the opposite side; and since, although each labyrinth can produce nystagmus in both directions, yet each has more influence in producing nystagmus to its own side than to the opposite one; it follows that if a patient with one labyrinth destroyed be turned towards the sound side, the nystagmus, *during* the turning, should be stronger than the nystagmus *after* the turning, while the reverse should be the case if he be turned towards the diseased side. In practice this has been repeatedly shown to occur; owing, however, to the difficulty of accurately observing the nystagmus *during* turning, it is more convenient to examine only the nystagmus *after* turning in either direction, when it is found, as would be expected, that the nystagmus, after turning to the diseased side, is more intense than the nystagmus after turning to the sound side.

(*b*) Syringing with hot and cold water.—By this method Dr. Bárány has investigated some 200 persons, including normal individuals, cases of ear disease, and deaf-mutes. He employs a Hartmann's attic cannula, which is connected with a large (No. 10) Politzer's bag by means of a rubber tube. After the introduction of the cannula, the bag (previously filled with water

of a little above the desired temperature, to allow for cooling) is slowly squeezed by an assistant. In cases with intact drum-head the cannula is inserted to the depths of the meatus; in those with a perforation, the end of the cannula is placed near to this or through it, and when the drum is completely absent the cannula abuts on the wall of the labyrinth. The duration of the latent period, that is, the time between the commencement of the syringing and the appearance of the nystagmus, is considerably increased by the presence of an intact membrane. The following results are obtained under normal conditions. (1) If water at the temperature of the body be employed, neither nystagmus nor any of the other signs of vestibular stimulation make their appearance, however long the syringing be continued. (2) If, on the other hand, the head being in the upright position, cold water, that is, water at a temperature below that of the body, be used, the result is a nystagmus directed to the side opposite to that of the ear syringed, this nystagmus being partly a horizontal, but mainly a rotatory one. (3) Lastly, the employment of water above the body temperature gives rise to a rotatory nystagmus towards the side of the syringed ear. The nystagmus, in this case, is usually weaker than that produced by cold water, for the reason that it is impracticable to make the difference between the temperature of the water and the body temperature so great with hot as with cold water; and it is upon this difference of temperature that the stimulation depends. It need hardly be remarked that the possible difference is still further diminished when the patient's temperature is above the normal.

An interesting point in regard to this caloric nystagmus is the fact that its character can be altered by a change in the position of the head, such alteration being sometimes not very clear, but when present, always of a typical nature. If, with the head upright the right ear is syringed with cold water, the result is a slight horizontal and marked rotatory nystagmus to the left side. If now during the syringing (or even in some cases after the discontinuance of it) the head be bent to the left shoulder, there appears a pure horizontal nystagmus to the right side, while the previous combined nystagmus to the left side becomes much weaker or disappears entirely. Further, on bending the head to the right shoulder, a pure horizontal nystagmus to the left side is produced; while if the head be completely inverted, so that the vertex is directed downwards, the result is a rotatory and slight horizontal nystagmus to the right side, that is, the direct opposite of that with the head upright. Again, if the right ear be

syringed with warm water the rotatory nystagmus to the right side, which is present with the head erect, changes on bending the head to the left shoulder to a left horizontal nystagmus, and on bending the head to the right shoulder to a right horizontal nystagmus, while complete inversion gives a rotatory nystagmus to the left side.

In addition to the nystagmus, syringing with hot and cold water gives rise to other symptoms of vestibular stimulation, such as reaction movements and vertigo, and it is worthy of notice that the same effects may often be produced by simple instillations into the external auditory meatus of fluids at a temperature different from that of the body.

There appears to be little doubt that the cause of caloric nystagmus lies in the production of convection currents in the endolymph, as a result of the partial cooling or warming of the latter. When the ear is syringed with cold water, the endolymph in contact with the tympanic wall of the labyrinth becomes cooler and tends, in virtue of its raised specific gravity, to fall, while the endolymph in contact with the inner wall of the labyrinth tends to rise; in this manner a stream is produced, having a definite direction. The application of warmth instead of cold will, of course, give rise to a stream in the opposite direction. These convection currents are capable of stimulating the ampullæ exactly as are the movements of the endolymph produced by turning, and the variety and direction of the nystagmus evoked, depends upon the particular canal affected and the direction of the current. Alteration of the position of the head alters the canal affected, and so changes the character of the nystagmus. With the head inverted the current is necessarily in the opposite direction to that with the head upright, hence, as might be expected, the nystagmus is reversed.

In actual practice it may be said that, when syringing with cold and hot water gives a perfectly normal reaction, the canal apparatus is functionally intact; should it be possible in such a case to demonstrate the existence of a fistula, a conclusion as to the strictly limited extent of the disease would be unavoidable. Such a case is described by Dr. Bárány on page 72 of his paper. The absence of any reaction with syringing furnishes definite proof of absence of function of the vestibular apparatus, and in association with middle ear suppuration points with great probability to involvement of the labyrinth. When together with unilateral ear disease there already exists a strong spontaneous nystagmus to the sound side, weakening of this nystagmus on

syringing the diseased ear with hot water will indicate that the labyrinth of this side is not completely without function, while if the syringing has no effect it may be concluded that the labyrinth is destroyed. Further, in a case of bilateral ear disease with spontaneous nystagmus to one side only, for example, the right, information as to the function of each labyrinth may be obtained by syringing the right ear with cold and the left ear with hot water, and endeavouring to detect any weakening of the already existing nystagmus.

(*c*) The galvanic current.—This method of stimulation may be applied in various ways, but Dr. Bárány prefers to employ a large electrode held in the hand of the patient while a small one is placed in contact with the tragus of the ear under investigation. A current of 10-15 m.a. is necessary, and the patient's gaze must be turned in the required direction. It is found in normal cases that with the anode applied to the tragus there results a rotatory nystagmus (with slight horizontal component) directed to the opposite side; while with the kathode applied to the tragus, a nystagmus having the same character, but directed to the side under observation, is produced. In addition there occur the reaction movements corresponding to the nystagmus. It is not yet certain whether the galvanic current influences the cristæ ampullarum, the nerve ends in the cristæ, or the twigs of the vestibular nerve at their entrance to the ampullæ. In cases of unilateral ear disease this method furnishes confirmatory evidence as to the condition of the labyrinth; if the latter is destroyed no nystagmus results from the passage of the current with the electrode applied to the diseased ear. Further, in a case with nystagmus already existing, the galvanic current may supply important information in view of the fact that the artificial production of a corresponding nystagmus should increase, and of an opposite nystagmus should diminish, that already present.

(*d*) Alteration of the air pressure in the external auditory meatus, and direct pressure on the stapes or a labyrinth fistula.—Gellé was the first to observe the production of vertigo by increase of the air pressure in the external auditory meatus; he did not, however, mention the occurrence of eye movements. Nystagmus and reaction movements may be elicited by any of the above methods in cases where the stapes is abnormally movable or a fistula of the labryinth is present, perhaps also in cases where the irritability of the vestibular apparatus is greater than normal. Since the direction of the flow of the endolymph is not under control, the direction of the nystagmus varies, being now to one side, now to another.

In connection with the functional tests in disease of the vestibular apparatus, some of the results of a sudden injury or destruction of the labryinth, such as may occur during an operation, are of great interest. In reference, in the first place, to cases of one-sided injury, Dr. Bárány considers it probable, on analogy from what is observed in animals, that at the first moment after the infliction of the injury, there occurs, as the result of the irritation of the affected labyrinth, a nystagmus towards the injured side. This, however, has not been definitely observed, and it is certain that a few minutes after the injury has been inflicted there exists a very intense spontaneous rotatory and horizontal nystagmus towards the sound side. It is believed that this nystagmus is caused by the vestibular organ of the sound side, the physiological "tonus" of which is no longer opposed by that of its fellow of the opposite (injured side). Further, should the injury have stopped short of complete destruction, the influence of the labyrinth of the sound side, in producing nystagmus towards its own side, may be to some degree aided by that of the injured side, for, as has been already remarked, each labyrinth can give rise to nystagmus to both sides.

For a short period after the injury the affected labyrinth may remain to some degree susceptible to stimulation by hot and cold syringing; this sensitiveness may in some cases persist, in others however it disappears and soon no reaction by syringing is obtained. But it is important to note that even in this stage direct pressure upon a fistula may produce nystagmus, and that the galvanic current may still give, for a time, a perfectly normal reaction. In this case it must be concluded that, while the conditions necessary for the production of endolymph currents are partly or wholly absent the vestibular nerve itself is still intact and capable of stimulation, and in favour of this view is the fact that the susceptibility to the galvanic current decreases much more rapidly after complete destruction of the membranous than after simple opening of the bony labyrinth.

It has frequently been observed that, after unilateral injury to the labyrinth the patient lies in bed on the sound side in preference to the injured one. This is probably to be explained by the consideration that in this position the patient, owing to the proximity of the pillow to the sound side, tends to look away from that side and towards the injured one. Now, since the nystagmus is most marked on looking towards the sound side, and since with the nystagmus are mainly associated the unpleasant sensations of nausea and giddiness, the maintenance of the position mentioned affords the patient most relief.

The disturbance of balance which is at first very marked and easy of demonstration, usually disappears rapidly, and may be entirely absent, while the nystagmus is still intense. In some persons, however, of strongly neurotic tendencies its presence has been observed months after the injury, a condition which Dr. Bárány regards entirely as a neurosis, the more so as the loss of balance is of an irregular and atypical character.

The nystagmus remains intense for some two to five days after the injury, and then decreases rapidly, but may be present in a slight degree weeks or months later, and is then often directed to both sides. Before this stage is reached the affected labyrinth has, of course, become quite insusceptible to any form of stimulation. It has been noticed also in some cases that, after the cessation of the early intense nystagmus, the labyrinth of the sound side seems to have become less sensitive to stimulation than was formerly the case.

No cases of bilateral injury to the labyrinth have been observed, but to judge from analogy with the unilateral cases, there would at first be signs of irritation, with resulting nystagmus to both sides. The nystagmus would then gradually decrease as would also, though probably more slowly, the sensitiveness to the galvanic current. The signs of complete bilateral destruction of the vestibular apparatus in man, as seen in cases of middle ear disease with involvement of the labyrinth, are those of total insusceptibility to all forms of stimulation.

The complicated nature of the subject, the literature of which is considerable, has made it impossible in the present short paper to do more than pass in review some of the more important of the results hitherto obtained. The behaviour of the vestibular organ both in health and disease, is however a matter not only of great scientific interest, but of considerable practical importance; and there appears to be full justification for Dr. Bárány's plea that in any case of middle ear disease, in which there is a question of the involvement of the labyrinth, the examination should include, in the first place, a careful determination of the presence or absence of nystagmus on lateral deviation of the eyes, and with the head in different positions; and, in the second place, an examination of the function of the vestibular organ by all the means of stimulation at our disposal.

THOMAS GUTHRIE.

Lehrbuch der Nervenkrankheiten für Aerzte und Studirende, von Prof. D. H. OPPENHEIM. Fourth Edition. S. Karger, Berlin, 1905. Two vols.

WHEN a text-book has reached its fourth edition and the second edition of its translation into English, it is a sure proof that it not only fulfils a want but that it also fulfils this want very successfully.

It will not be necessary to describe in detail the arrangement of the work as it follows that of most other text-books on the subject, beginning with the description of the methods of examination, and then taking the diseases of the spinal cord, peripheral nerves, the brain, the neuroses, diseases of the sympathetic, and those of intoxication.

Throughout the work, we have the most recent knowledge on the subject.

Under disorders of sensation we have notice of Head's work on referred pain, and we have also new terms introduced, bathyanæsthesia, pallanæsthesia, *i.e.*, loss of vibration sensation in bone, and macroæsthesia. The anatomical description and the physiology of the spinal cord is good, and especially the question of the reflexes is very well described.

On the sensory areas corresponding to the different segments of the cord Prof. Oppenheim has taken Seiffer's scheme, but this does not give any differentiation between the areas supplied by the sixth and seventh cervical, or eighth cervical and first dorsal roots.

Brown-Séquard's paralysis and the difficulty of reconciling it with some recent experiments is discussed. Under the heading tabes we have the use of cyto-diagnosis with lumbar puncture. Injection of cocain into the subarachnoid space for tabetic pains and gastric crises is mentioned, but we do not find any account of the importance of preventing cystitis and of treating it by irrigation of the bladder; this is evidently an oversight, but as vesical troubles are the most dangerous to life in tabes we think that this should be impressed on the student. Under poliomyelitis anterior acuta the latest observations on the part played by micro-organisms in producing the disease are given, and in peroneal atrophy the degeneration of the posterior columns, lateral columns, anterior roots, &c., which have recently been observed. In myelitis reference is made to the theory that thrombosis produces an area of less resistance, which is then

attacked by micro-organisms, streptococci, staphylococci, and pneumococci.

The pathology of disseminated sclerosis is discussed, as to whether the disease starts in the nerve elements, the neuroglia or the perivascular lymph spaces on the arteries. Following the brilliant case of Gowers and Horsley, the treatment of spinal tumours by operation is fully considered. Under Landry's paralysis we have the finding by Chantemesse and Raymond, and of F. Buzzard, of organisms, which produce paralysis when injected into other animals. Both Landry's paralysis and craft palsies (Arbeitsparesen) are included under diseases of peripheral nerves, while occupation spasms (Beschäftigungskrämpfe) are included under the neuroses.

In vol. ii. the Anatomy and Physiology of the Brain is well described, including Grünbaum and Sherrington's recent work on the anthropoid brains, with a reproduction of their figure of the motor centres on the chimpanzee's brain. Under hemianopsia we cannot find any reference to quadrantanopsia as it occurred in Hun's well-known case. Under hemiplegia we note that mention is made of Babinski's observation on paralysis of the platysma in organic but not in functional hemiplegia, and also that according to Widal we can make certain from lumbar puncture and the indication obtained by lymphocytosis that the disease has a syphilitic basis. The relation of acute hæmorrhagic encephalitis to otitis purulenta, bronchiectasis, septicæmia, malaria, meningo-encephalitis is discussed, as also the most recent opinions on the intrauterine and post-partum causes of porencephaly.

The chapter on cerebral tumours is exceedingly good. On the treatment of cerebellar tumours by operation, although Prof. Oppenheim expresses the opinion that the chances of cure are very slight, he gives full credit to the successful results of Horsley, Ballance, and other surgeons. In the pathology of myasthenia gravis, he thinks that the factors are congenital abnormalities, and also developmental anomalies, such as persistent thymus gland and thymus tumours, which bring toxic products into the circulation, and so cause a metastatic disease of the muscles.

In the chapters on the pure neuroses, in discussing autointoxication as a cause of epilepsy, he does not think that we are justified in regarding the theory as firmly established; the treatment advocated by the followers of this theory would consist of purgatives, diuretics, lithium carbonate, and intestinal antiseptics. The treatment of epilepsy is well given, but we cannot gather that the author gives any preference to any par-

ticular salt of bromine. He refers favourably to the treatment with bromides and with omitting table salt from food, but he is not in favour of the opium and bromide treatment, as he considers it to be not without danger, an opinion with which we should agree. We should also agree with him as to the conditions under which operations for epilepsy are advisable. In chorea he considers that electrical treatment is of doubtful benefit. In the pathology of paralysis agitans he mentions the changes found in the muscle-fibres and muscle-spindles by recent authors, and the relation of the disease to the thyroid gland, and he quotes a case treated by thyreoidin but without any effect. We strongly agree with him that harm may be done in the treatment of this disease, and that all vigorous treatment should be avoided. He further states that forcible water cures, electricity and massage are no good—though he has seen good from the electric bath—and he finds little benefit from the shaking chair. In the treatment of exophthalmic gôitre, favourable results are quoted from serum, and from a powder made from the milk of animals from which the thyroid has been removed; and also of Kocher's treatment by removal of part of the thyroid gland, or by ligature of some of its arteries.

Throughout the work the references to other authors is very complete, and it would have added considerably to its usefulness as a work of reference if the title of the paper from which the reference was made was given as a foot-note. There is one curious omission in the case of exophthalmic gôitre, for though it is stated in the text that the disease was described by Graves in 1835, and eight years later by Basedow, in 1843, the section in the book is called "die Basedowsche Kranheit." If it is not to be known as Graves' disease it had better be called exophthalmic gôitre.

The illustrations are numerous and good, and we would particularly commend fig. 373, illustrating tetany. The book well maintains its position as the standard text-book of neurology in Germany, and we congratulate Professor Oppenheim on his work, which is worthy of the high reputation of the important school of neurology in Berlin.

C. E. Beevor.

Tumours of the Cerebellum. By CHARLES K. MILLS, M.D.; CHARLES H. FRAZIER, M.D.; GEORGE E. DE SCHWEINITZ, M.D.; T. H. MESSENBERG, M.D.; EDWARD LODHOLZ, M.D. New York: A. R. Elliott Publishing Co., 1905.

THE account of the symptomatology of tumours of the cerebellum, by Dr. Mills, follows closely the classic descriptions of Luciani and Risien Russell. There is an absence of conciseness and a lack of perspective as to the relative importance of symptoms which tend to leave a sense of confusion with the reader. No reference is made to such important symptoms as forced movements, compensatory attitudes, the condition of static equilibrium and the diadococcinesia of Babinski. It would have helped the reader considerably if certain statements concerning symptoms had been qualified and explained instead of being placed before him as facts. Thus, in dealing with vertigo as a symptom Dr. Mills writes: "The vertigo, which is so frequently a symptom of brain tumour, wherever situated, is usually due to irritation of branches of the trigeminal nerve, which are distributed near the inner surface of the dura, the irritation of the fifth nerve being reflected to the latter nuclei of this nerve and thence to the pneumo-gastric nucleus."

Again, when dealing with differential diagnosis between prefrontal growths and cerebellar growths, he writes: "When a prefrontal growth is situated on the left, mental symptoms of a distinctive character are present." Surely so sweeping an assertion would be more acceptable if the reader were told what these distinctive mental symptoms are.

Dr. Mills writes further: "Convulsions, unilateral or general, but more commonly the latter, with unconsciousness, have occurred in a considerable percentage of my cases." There is no statement as to the stage of the cerebellar disease at which such convulsions occurred, nor as to the presence of hydrocephalus, nor of severe symptoms pointing to general increase of intracranial pressure. From the immediately preceding sentence and from the entire absence of subsequent qualification, convulsion appears as a cerebellar symptom.

In certain cases the presence of incontinence of urine and of fæces were present apparently as symptoms referable to the presence of the tumour on the cerebellum. This is a remarkable

and valuable clinical fact. But the succeeding sentence that incontinence occurs in connection with cerebral tumours, regardless of situation, and only when the patient is mentally or physically *in extremis*, is far from the experience of the many who have recorded early incontinence in connection with prefrontal and temporo-sphenoidal lesions.

If we ask Dr. Mills how to determine whether a tumour is acting as an irritative or destructive lesion, he directs us to find the answer in a study of the spastic (irritative) or non-spastic (destructive) condition of the limbs of one side and a careful consideration of the side to which the eyes are turned (conjugate deviation to the same side). Nothing could be simpler nor more satisfactory than this answer were we told how to recognise these distinctive spastic signs, and were it not that other writers upon this subject have not found that unilateral rigidity and conjugate deviation are manifestations of cerebellar lesions. In this connection, why does Dr. Mills entirely ignore forced movements, which are almost universally considered to be pathognomonic cerebellar signs?

In his use of the term Romberg's sign, the writer infringes tradition. He writes: "The Romberg symptom is practically always present. . . . it is much less markedly increased by closing the eyes than in tabes. . . . But unless the cerebellar disease is much advanced a patient will often be able to keep relatively steady with the eyes shut for a considerable time."

Such confusion and contradiction occurring in more places than one detract much from this fragmentary and obsolete account of the clinical aspect of cerebellar disease.

Proceeding to the surgical aspect of tumours of the cerebellum one finds an exceedingly clear and concise description by Dr. Charles H. Frazier. He lays great stress upon the necessity of early operation in cerebellar tumour as compared with cerebral tumour, if favourable results are to ensue; the increased supratentorial pressure which is apt to come on early being a condition most unfavourable to success.

While all agree as to the impossibility, in most cases, of locating, even approximately, the position of a lesion of the cerebellum, and that the space for search and manipulation in operation is very small, yet Dr. Frazier's opinion that it is better to remove the cerebellum freely, both in exploring and in removing tumours, than to risk any pressure upon the medulla and bruising, is an opinion with which many will dissent.

Puncture of the ventricles to relieve pressure and give more room for manipulation is condemned on account of its frequent and rapid fatal consequences; neither has lumbar puncture proved of value. Ligation of the lateral sinus is a procedure which is absolutely unjustifiable, as it adds greatly to the risk.

Especially interesting is the operative technique for exploration of the cerebello-pontal angle. It is to be regretted that Dr. Frazier does not mention the position in which his patient is placed for operation, nor is the way in which the head rest, which he recommends is to be used, clear, neither from the figure nor the text.

In his excellent article Dr. Frazier must be convicted of one glaring error. He writes: "It should be borne in mind that under normal conditions the cerebellum is under greater tension than the cerebrum." Now this is, in the first place, a physical impossibility, since the intracranial pressure is a fluid pressure, and is a "factum" of the blood pressure, and in the second place, such a condition of unequal pressure would not allow of the flow of cerebrospinal fluid from supratentional to infratentional ventricles.

Dr. de Schweinitz describes the ocular symptoms. Dealing with the frequency of occurrence of optic neuritis in relation to the position of intracranial growth, he refers to the analysis by Dr. John Weeks of 677 cases of brain tumour, the result of which analysis is that optic neuritis is formed most frequently in growths situated on the mesencephalon 100 per cent., parieto-occipital region 87·8 per cent., cerebellum 87·2 per cent. An unqualified statement of this nature is most misleading. Among the 677 cases how many tumours of the mesencephalon were there? Many of the highest authorities hold that optic neuritis is more often absent in cases of mesencephalic tumour than in cases of intracranial tumour in every other situation, the pons variolii not excepted.

When discussing the time at which optic neuritis is recognisable after the presumed time of commencement of the lesion, Dr. de Schweinitz writes that, "the neuritis may appear within a few weeks, or even within a few days after other signs of involvement are evident; for example, intense headache, vomiting and vertigo. Sometimes longer periods of time are required before optic neuritis is discovered." In this statement there is the obvious objection that intense headache and vomiting are extremely rare in cases where optic neuritis is absent. Local signs may exist without general signs, but of the general signs optic neuritis is surely the first to appear.

Unilateral optic neuritis or great inequality in the degree of neuritis in the two eyes, is held by the writer to indicate that the lesion is upon the side of the greater papillary change, and that such inequality is in favour of the tumour being supratentional rather than infratentional. An intense and rapidly occurring neuritis points to a cerebellar situation of the tumour. In a book, of which the special object is to urge early operative interference in cerebellar tumour, it seems a pity that unqualified prominence is given to such fallacious physical signs. Cases which prove these rules are only slightly more common than cases which form exceptions, and, therefore, the rules must be entirely disregarded in localisation.

The writer's opinion upon the effect of operation upon papillitis is most interesting. The effect is much greater in simple "choked disc" than when inflammatory retinitis is present. Trephining without removal of the tumour acts as an important palliative measure, but he does not mention whether the dura must be opened to produce the palliative effect.

Ocular paralyses are considered as due either to pressure effects upon the nerves, or to associated involvement of the pons or mesencephalon. The "skew deviation" is mentioned without discussion. Nystagmus, with slow movement to side of lesion is commonly the sole ocular sign of cerebellar growth.

Upon the difficult subject of the pathology of cerebellar growths, Dr. Weisenberg writes an excellent essay. "Gummata are extremely rare in the cerebellum." "Gummata are rarely found *post mortem*, although they are possibly the most common cervical growths." Is Dr. Weisenberg deferring to the opinion of clinicians in this last remark? Since the rarity of intracranial gummatous tumour at autopsy is the universal experience of pathologists, upon what evidence does its occurrence as emphasised by clinicians rest. Since a very large proportion of subjects who develop symptoms of cerebral tumour, die as the result, and since those cases in which anti-syphilitic treatment removes the symptoms most often die later on from a recrudesence of such symptoms, and upon autopsy non-syphilitic tumours are found, and since it is a well-known fact that intracranial tumours may become quiescent, one cannot but think that the frequency of syphilitic tumour of the brain is a widely prevalent notion without proved basis of fact.

The evidence which the writer brings forward of the existence of symptoms of cerebellar growth without lesions is altogether unconvincing, for in no case was the absence of a lesion verified

by *post-mortem* examination. Two of the verified cases, fibroma of the floor of the fourth ventricle and sarcoma of the floor of the fourth ventricle, with hydrocephalus are certainly not cases from which the absence of lesion of the cerebellum can be argued.

As little conclusive as the foregoing is the evidence of the existence of cerebellar lesions without symptoms, for it is well-known that cerebellar symptoms may be temporary or transient, or may be masked by symptoms due to hydrocephalus, and, further, that cerebellar lesions may become quiescent.

Dr. Lodholz describes the functions of the cerebellum. In reality he vigorously attacks all the theories that have been advanced as to cerebellar function. He takes as his text Wundt's statement, "the functions of the cerebellum belong to the darkest part of the central nervous system" and leaves his reader with one undisputed fact only, which is "the cerebellar cells are continually exerting an influence upon other nerve-cells, but of the true nature of this action nothing is known with certainty." This does not appear to be the happiest ending to a volume of which the aim is to aid the early recognition of the phenomena resulting from disturbance of cerebellar function.

J. S. Collier.

Publications Recently Received.

[*Notes on a book under this heading do not preclude a subsequent review.*]

Jahresbericht über die Leistungen und Fortschritte auf dem Gebiete der Neurologie und Psychiatrie, ix. Jahrgang. Bericht über das Jahr 1905, pp. 1291. Berlin: S. Karger, 1906.

This wonderful compilation should be on the shelves of every neurologist. The abstracts are remarkably accurate and complete, and the orderly arrangement of the work saves much time and labour. A paper dealing with several subjects appears under each separate heading, so that it cannot be missed, even if the reader happens to consult the section dealing with a subsidiary part only of any particular paper.

Medical Electricity. By H. LEWIS JONES, M.D. 5th Edition. London: H. K. Lewis, 1906.

The fifth edition of the well-known handbook has been to a great extent re-written. The chapter on X-rays has been expanded and much interesting matter added to almost every chapter. For students and practitioners who are interested in the subject of the application of electricity to medicine it is invaluable.

Diseases of the Nervous System resulting from Accident and Injury. By PEARCE BAILEY, A.M., M.D. London: Sidney Appleton, 1906.

This is an extension of the author's work on "Accident and Injury in their Relation to the Nervous System." He claims that it is written from the neurologist's standpoint, but judged by this standard the information is meagre. He deals with the great question of concussion of the brain in a little over eleven pages of large print. To the focal diagnosis of injuries to the spinal cord he brings no first hand cases and accepts Seiffer's diagram of spinal segmentation without discussion. Injuries to the peripheral nerves are treated as if everything had long been known about their distribution and function. The most useful portion of the book deals with the relation of trauma to such diseases as dementia paralytica, tabes dorsalis and progressive muscular atrophy.

Die Röntgenstrahlen im Dienste der Neurologie. Von Dr. WILHELM FÜRNROHR. Pp. 375, with 29 illustrations. Berlin: S. Karger, 1906.

This book deals with the application of X-rays to the study of diseases of the nervous system, particularly those where morbid changes can be detected in the bony structures surrounding it. Spina bifida, acromegaly, tuberculosis of the vertebræ, and many other conditions are considered, together with the changes in the bones and joints which occur in nervous disease. The diagnosis of cerebral hæmorrhage and cerebral tumours is also considered.

X-rays in General Practice. By A. E. WALTER, M.D., Captain, I.M.S. Pp. 175, with 118 illustrations. London: John Lane, 1906.

A short account of X-ray apparatus and methods, with some interesting details of X-ray work under Service conditions in India.

Studien über Poliomyelitis Acuta. Von Ivar Wickman. Berlin: S. Karger, 1905.

A valuable account of seven cases in which a complete *post-mortem* examination was carried out on patients dying at from three to eight days after the onset of poliomyelitis. The figures are excellent. The author reviews the whole modern standpoint with regard to this disease, and compares the pathological process with that in acute myelitis.

Archives of the Pathological Institute of the London Hospital. Vol. i. London: Adlard and Son, 1906.

This volume of reports contains one paper of interest to neurologists on a case of poliomyelitis acuta. A child of 4 years was admitted to the London Hospital and died on the seventeenth day of the illness. The onset was sudden with convulsions and the left arm and leg gradually became paralysed. At the autopsy the whole of the right hemisphere in the motor region of the cortex was found to be connected with soft greyish pulp, much of which was fluid and drained away on incision. The contents of this softened area were not purulent. A careful microscopical examination was made.

Die Nervosität, ihre Ursachen, Erscheinungen und Behandlung. Von Dr. A. Cramer. Pp. 424. Jena: Gustav Fischer, 1906.

This book is admirably arranged; causes and symptoms are mentioned one by one in the first two chapters; then follows a third part devoted to neurasthenia and hysteria. The book closes with a section on treatment. In the margin of the page, beside each paragraph, the content is indicated, so that it is unusually easy to find any one symptom or sign of which the reader is in search. The list of subjects touched on is so complete that discussion and description are frequently curtailed to a length which renders the work of less use to the trained neurologist than to the general physician. But to him this work can be recommended, especially if he is anxious to amplify his knowledge.

Clinical Lectures on Neurasthenia. By Thomas D. Savill, M.D. 3rd (revised and enlarged) Edition. Pp. 216. London: Henry J. Glaisher, 1906.

The author holds that about 80 per cent. of cases of neurasthenia are due to "some kind of intoxication (toxæmia)." He

attempts to differentiate "cases of cerebral neurasthenia and neurasthenia insanity" from "typical cases of true insanity." Among the cited cases are most of the usual forms of this disease met with in practice; but the book will add little to the knowledge of the professed neurologist, and is too diffusely written for the general practitioner.

Die Kontracturen bei den Erkrankungen der Pyramidenbahn. Von Dr. OTFRID FÖRSTER. Pp. 65. Berlin: S. Karger, 1906.

A careful and thoughtful analysis of contractures, following disease of the pyramidal tracts, by the author of the well-known book on coördination. Well worthy of careful study.

Paralysie Générale et Syphilis. Communications faites à l'Académie de Médecine. Par MM. ALFRED FOURNIER and F. RAYMOND. Pp. 100. Paris: Masson et Cie, 1905.

The Académie de Médecine devoted several sittings to the question of the relation between syphilis and general paralysis of the insane. Here we find all that was said by the two great supporters of the direct relation of these two diseases to one another.

Die Polyneuritischen Psychosen. Von Dr. ALBERT KNAPP. Pp. 144. Wiesbaden: J. F. Bergman, 1906.

An account of eight cases, with a short description of the various symptoms which may accompany multiple neuritis. Its various psychical accompaniments are classified and described shortly.

Über Störungen des Handelns bei Gehirnkranken. Von Professor D. H. LIEPMANN. Pp. 161. Berlin: S. Karger, 1905.

An interesting discussion of defects of function, due to disease of the highest centres. Mental and physical disturbances are dealt with on the same principles. The author discusses varieties of disturbed action, Wernicke's views, ideational and motor apraxia, and ataxia. The book is unusual in that the facts already known to the readers of neurological literature are considered, as a whole, psychologically, without the repetition of clinical details.

Studies in Clinical Psychiatry. By LEWIS C. BRUCE, M.D. Pp. 246. London: Macmillan & Co., 1906.

The author has attempted to examine the more acute insanities from the point of view of modern views of bacterial infection and toxæmia. Among these he places excited melancholia, acute mania, folie circulaire, katatonia, hebephrenia. He supports his view by many charts and observations, showing the leucocytosis which accompanies these diseases. The reaction to vaccines is also discussed. In several instances the urine was examined more completely than is the case, even in hospital practice.

The Subconscious. By JOSEPH JASTROW. Pp. 549. London: Archibald Constable, 1906.

The first part of this book is taken up with a consideration of the phenomena of consciousness in the normal individual. Throughout the second part abnormal states are described and disintegrated personality is discussed. The third part is theoretical. This book contains no new observations; but the second part will help the neurologist to formulate his views on the difficult subject of altered personality.

Atlas der Pathologischen Histologie des Nervensystems. Redigirt von Dr. VICTOR BABES. iii. Lieferung. "Histologie des lésions expérimentelles et pathologiques des cellules nerveuses surtout des ganglions spinaux.' Par V. BABES et G. MARINESCO. Pp. 35. Berlin: August Hirschwald, 1906.

A paper by the two above-named authors on the minute structure of the nerve-cell, illustrated by a series of beautiful plates. This forms the third part of the atlas, which is now complete in nine parts. A very beautiful work.

THE NEUROLOGICAL SOCIETY OF THE UNITED KINGDOM.

At the Meeting held on Saturday, July 14, at the National Hospital, Queen Square, at 10.30 a.m., the following cases and specimens were exhibited:—

Dr. W. J. Potts.—*A case of Friedreich's disease with onset late in life.*

Family history.—The family originally consisted of five members:—

(1) *Edward.* Died at Bethnal Green Infirmary four months ago at the age of 40. Affected with the disease; its first symptoms occurred at about 32 years.

[Pathological specimens on exhibition by Dr. Gordon Holmes.]

(2) *Mary*, aged 39, an in-patient at Bethnal Green Infirmary. Affected with the same disease in an advanced stage; onset at about 36 years.

(3) *Arthur*, now 36 years of age. Healthy.

(4) *Ernest*, aged 34. Now shown to the Society.

(5) A brother who died at the age of 10 from fits.

No other relatives known to have suffered similarly.

Ernest H., boot clicker, aged 34.

History.—Onset gradual; first noticed speech affected about seven or eight years ago, and a little later that his gait was affected. Worked till two years ago, but had noticed for some years that he could not work as fast as he used to do; symptoms of weakness of upper extremity followed shortly after gait was affected.

Present condition.—*Cranial nerves.*—Speech syllabic and slightly high pitched. No ocular paralysis, retinal defect nor nystagmus. Mental condition good.

Upper limbs.—Muscular nutrition fair; incoördination of arms and hands present, but not excessive. Slight hyper-extension of fingers. Sense of position good. No anæsthesia nor analgesia.

Trunk.—Lateral curvature of spine with convexity to right in upper dorsal region. Superficial reflexes diminished.

Lower limbs.—Muscles small, strength diminished. Slight incoördination of movement. *Gait*—Well-marked ataxia, especially in turning; slight spastic element; Romberg's sign present. No deformity of feet. Knee-jerks absent, as also Achilles-jerk; Babinski's extensor response well marked on the right side, less definite on the left. Cutaneous sensation good. Sense of position decidedly impaired. No sphincter trouble.

Dr. Fred. S. Palmer.—*Friedreich's ataxia ?* (*advanced stage*) *with an interesting family history.*

E. D., aged 16, admitted to the West End Hospital on May 2, 1906.

The patient (a twin) is the youngest of eleven children, of whom two (twin girls) were stillborn. Three (boys) died in childhood, and six (girls) are living.

Both parents (first cousins) are alive, and well; no evidence of direct heredity, epilepsy, nor cerebral disease, can be obtained on either side. Of the surviving members of the family, two sisters, aged respectively 34 and 29, are married, and each has three children, apparently quite well. Another, aged 31, is in the Bancroft Road Infirmary, said to be paralysed; one, aged 24, is at home paralysed and unable to feed herself without assistance, and another is in an Asylum at Epsom.

The patient was perfectly well and hearty until she had an attack of so-called Rötheln at 5 years of age. During convalescence, it was noticed that her lower limbs were very weak, and that she frequently staggered and fell in attempting to walk. Since then the disability has been steadily progressive. Her speech first became affected two years ago, when her menstrual periods commenced. Her intelligence is below the normal, but her memory is said to be fairly good. At the present time she is quite unable to stand without assistance. Her speech is slow, laboured and very indistinct. There are slight nystagmoid movements on lateral deviation, but no paresis of the ocular muscles. She has mixed astigmatism in both eyes, with some degree of pallor of the discs. There is considerable weakness and incoordination of both upper limbs with marked muscular atrophy, more especially in the small muscles of the hands, and she exhibits the *main en griffe*, but there are no choreiform movements nor fibrillary tremors to be noticed. The supinator jerks are not obtained. Some deviation is observed in the dorsal spine,

probably from weakness and wasting of the muscles, but there is no rotation. Both lower limbs are paralysed and the muscles are small. Her feet show the rectangular form of equinus with some slight degree of pes cavus. The knee-jerks are abolished; there is no ankle clonus, but the plantar reflexes are of the extensor type. Her sphincters are not affected, nor is there any change in the tactile sensation.

Dr. JAMES TAYLOR.—*A case of Friedreich's disease, with double optic atrophy.*

K. P., aged 27, first came under observation in 1904. He has a sister, three years older, similarly affected, but without optic atrophy.

From childhood he never was able to walk properly, and since the age of 18 he has not been able to walk at all. The more obvious symptoms of his affection were remarked when he was about 16 or 17 years old, viz., unsteadiness of arms, peculiarity of speech, failing eyesight, rolling movements of eyes, weakness and stiffness of legs.

He presents the cardinal features of the disease, such as scoliosis, pes cavus, nystagmus, slow slurring articulation, great weakness and considerable wasting of the musculature, coupled with hypotonia, tremor and incoördination of limbs, involuntary spasms in legs, absence of all reflexes, double extensor response.

He presents a mental condition not infrequent in Friedreich's ataxia; he has double primary optic atrophy, with concentric contraction of the visual fields, and is unable to count fingers beyond a foot or two.

Dr. BUZZARD.—*Disseminated sclerosis and functional paraplegia occurring in two sisters.*

(1) E. S., aged 48, is a typical case of advanced spastic disseminated sclerosis.

About five years ago, her legs rather suddenly became heavy and weak when she was out walking At the same time they became numb. From that time she has steadily got worse, the legs becoming more and more stiff. She has had frequent and painful involuntary flexor spasms in the legs, paræsthesiæ in arms and legs, and some months ago weakness and stiffness of the left arm. During the last twelve months she has had frequent attacks of transient amblyopia, and, for the same time, precipitancy of micturition.

There is pallor of both optic discs, slight nystagmus, but no other cranial nerve symptom. The left arm is weak and stiff, and there is some wasting of the interossei. Both legs are in a state of extreme spasticity, and are immobile, or practically so, the effort to move them being usually interrupted by flexor spasms.

There is considerable diminution to touch and pain in the legs, and to a less extent in the left arm. Very active tendon reflexes, double ankle clonus and extensor response. The abdominal and epigastric reflexes are absent.

(2) F. S., aged 43, is a typical case of functional paraplegia.

She became ill about a year *before* anything was noticed wrong in her sister's case. The onset was apparently sudden, patient remarking that her legs were very stiff and heavy. The condition has continued with little change; the legs have become intensely stiff, and passive movements are almost an impossibility.

During the same time the legs have become numb. About a year ago she suddenly lost power in her left arm and hand, and this weakness continues. Paræsthesiæ in the same limb.

No diplopia nor amblyopia, no trouble with sphincters.

Optic discs are perhaps a little pale. No nystagmus.

In the legs the rigidity is found to be accompanied by defective inhibition of the antagonists of any given movement. If the leg be passively flexed and the patient asked to extend it the first movement is a sudden powerful contraction of the hamstrings, effectually preventing the accomplishment of the desired movement. This is true for all joints in the legs, and it accounts for the functional tremor of the left arm whenever she essays anything with it. Considerable diminution to touch and pain in legs and arms.

Abdominal and epigastric reflexes are brisk; knee-jerks are active; there is no ankle nor other clonus; no sphincter defect; double flexor response.

Gait is typically functional.

Dr. BEEVOR.—*Pseudo-bulbar paralysis.*

Sidney M., aged 23, soldier, had specific disease in 1900.

In July, 1903, suddenly without loss of consciousness, lost power in *left* face, arm and leg for two weeks. Speech indistinct. In November, 1903, lost power during sleep in *right* arm and leg, (?) face. Speech affected. He improved. In June, 1904, admitted into Great Northern Hospital, and had lost

power in left arm, leg and face, not unconscious, lost control of sphincters. Unable to phonate (but could groan), swallow or move soft palate, he could not open nor shut mouth, bite nor move tongue; he had to be fed by a nasal tube; he could not elevate angles of mouth, close mouth or eyelids, nor wrinkle brow. Eye movements normal, and could elevate brows. He could not voluntarily inspire nor expire, and could not give a voluntary cough, but could cough reflexly. Very emotional. In laughing both sides of face were retracted, but the left less than right; in yawning both sides moved equally (this would suggest that the movements of yawning and laughing are innervated from different parts of the central nervous system). The left arm and leg could perform all movements though weaker than on right. The left latissimus dorsi acted well in the unilateral movement of adducting left humerus, and in the bilateral expiratory movements of emotional laughing or reflex coughing, but neither side acted in voluntary coughing. The left knee-jerk was increased, and there was left extensor plantar reflex. In July, 1904, admitted into National Hospital, and could only just pronounce some vowels and could just swallow. He could not voluntarily perform defæcation, and had precipitate micturition. Has gradually improved, but not advanced much since eighteen months ago, when he could close eyes, show teeth, and just close mouth; could take a voluntary inspiration and expiration, and faintly cough. The lesion is considered to be bilateral, from specific thrombosis of the branches of the posterior communicating arteries which supply the anterior one-third of the posterior segment of the internal capsule. It is probable that the cortical fibres for voluntary inspiration and expiration, and for the inhibition of the vesical centre pass down on both sides through this part of the internal capsule. The important point is the bilateral paralysis of bilateral movements of the lower face and fauces, with paralysis of voluntary movements of respiration, with retention of the emotional and reflex movements, and with only slight weakness of the limbs.

(2) *Case of myasthenia gravis.*

Alice E., aged 24.

Symptoms began in the spring of 1901, with difficulty in swallowing. At the same time, she had occasional attacks of choking. About three months later, difficulty in chewing. She found about this time that her arms and legs were getting weak, and that she could not sustain muscular effort.

When she first came under observation, October, 1901, the ocular movements were affected, chiefly upward; after exercise there was greatly increased paresis with ptosis. Epiphora owing to the falling away of the lower lid. Facial movements restricted. Buccinators and masseters weak. Could not inflate her cheeks unless nostrils were held. Tongue could not be protruded nor curled up, and there was a central groove along it. Palatal movements were also weak, and there was difficulty in swallowing. Peripheral and trunk muscles were fair.

Seen again summer, 1903. Feeling of weakness and of rapid fatigue has steadily and progressively got worse.

In addition to previous account, bilateral ptosis, inability to close eyes tightly, internal strabismus, with paralysis of left rectus externus, obliteration of facial lines, eversion of lips, inability to purse up or close mouth, articulation nasal, almost unintelligible, phonation impaired, palate movements *nil*, wasting of edges of tongue, musculature generally somewhat shrunken, strength at first fair. All reflexes brisk.

Readmitted, February, 1906. Both eyes deviate conjugately to right when patient tries to shut her eyes. Respiration is almost entirely costal, diaphragm not acting. Three grooves on tongue, which is atrophic and tremulous. Flapping of the vocal cords on phonation. Lordosis in erect position. The lower fibres of pectoralis major are very atrophic, especially on the right, and require a stronger faradic current for their contraction and then only a faint flicker is obtained. Muscles show tiring by faradism after seventy contractions have been produced. Tiring not produced by repeated testing of knee-jerks. Unable to sit up without using arms. She has improved with rest in bed.

Dr. C. M. Hinds Howell.—*Three cases illustrating the effects of cervical ribs.*

C. A., a woman, aged 21, a milliner's assistant. Duration of symptoms two years; onset gradual.

History.—Two years ago began to notice pain and weakness in right hand when cutting wires with pincers or using scissors. Pain, severe at times, felt in hand and up the arm as far as shoulder, latterly pain confined to inner border of arm, and only felt occasionally.

Muscular condition.—Slight weakness of flexors of wrist and fingers, weakness of thenar and hypothenar muscles, interossei weak, especially the first dorsal. Wasting most marked in thenar, hypothenar and interosseal muscles.

Sensation.—Anæsthesia well defined in first dorsal distribution, pulses equal at wrist, pupils equal.

Electrical reactions.—Flexors of wrist and fingers normal. Diminution in faradic excitability in interossei; R.D. in thenar and hypothenar muscles.

X-ray photograph.—Double cervical ribs.

R. C., a girl, aged 14. Duration of symptoms four months. Onset of symptoms gradual.

History.—For last four months patient has complained of weakness of thumb of left hand. Ill-defined pain, aching in character for last six weeks, worse during last month, and felt especially along radial border of thumb.

Muscular condition.—Thenar eminence of left hand only affected. Wasting confined chiefly to abductor and opponens pollicis. Adductor pollicis showing only slight wasting. No other muscular weakness nor wasting.

Sensation.—No changes discovered. Pulses equal at wrist. Pupils equal.

Electrical reactions.—Partial R.D. in muscles of thenar eminence, except flexor brevis pollicis, which appears to have escaped.

X-ray photograph.—Cervical ribs, that on left side being much the more obvious in photograph.

G. T., a man, aged 37; occupation, carman. Duration of symptoms five years. Onset gradual.

History.—Gradual progressive weakness of left forearm and hand, never any pain in arm or neck.

Examination.—Obvious swelling in left posterior triangle of neck pulsation over this swelling, due to subclavian artery. Left arm less well developed than right, with marked wasting in forearm and hand.

Muscular condition.—Grasp very weak, with extension of wrist. Muscles on ulnar side of forearm much wasted, very little power in flexors of wrist and fingers.—Extensors of wrist and fingers weak, but much less affected than flexors.

Hand.—Thenar, hypothenar and interosseal muscles much wasted, *main en griffe.*

Pulses.—Left radial pulse much diminished. *Pupils* equal, react well.

Skin.—Over hand and lower half of forearm, cyanosed, particularly in cold weather.

Sensation.—Marked sensory loss in areas of first dorsal and eighth cervical; most marked in latter.

Electrical reactions.—Diminished excitability in extensors, more marked in flexors, absent in hand muscles.

X-ray photograph.—Double cervical ribs.

June 12.—Operation, cervical rib removed, pulses equal after operation.

June 27.—Definite improvement in sensation, chiefly in first dorsal distribution.

Dr. J. S. Collier.—*Case of possible vascular lesion of Optic Thalamus.*

Man, aged 55, arterio-sclerosis. Sudden onset of jerky tremor in left arm and leg six months ago, accompanied by mental perturbation. The condition has not changed since. Slight left facial weakness. Very slight left hemianæsthesia. No hemiplegia.

Dr. James Taylor.—*Case in which symptoms of intracranial growth were relieved by trephining.*

F. P., aged 11, sent to Dr. James Taylor, at Moorfields, by Mr. Lawford. Nothing significant in the family history. The father and mother are healthy, and there are two other children. The mother suffered from puerperal septicæmia after the child was born. At the age of 14 days it was noticed that she had some ear discharge. There was a recurrence of this at 2½ years of age, and it has been present intermittently since. The right ear was more severely affected than the left. In August, 1904, having been previously quite well except for the ear discharge, she began to suffer with headaches and vomiting. There was blood discharged from the ear. No loss of vision was noticed. On December 13 there was severe headache in the right occipital region, but also in the frontal region and in the vertex. In March, 1905, there was definite impairment of vision, more in the right eye than in the left. There was no loss of memory, no diplopia, and no indication of any other form of paralysis. There was intense optic neuritis. Operation was recommended on the chance of the symptoms being the result of a collection of pus in the brain. On May 13 there was an operation on the right side, but no abscess was found; and on May 23 there was a similar operation on the left side, with a similar result. On July 4 the right side was again explored, but nothing was found, although there was an escape of a little cerebro-spinal fluid. After the operation all her symptoms subsided, and the optic neuritis also disappeared.

She has since remained perfectly well, except for slight deafness, the result of the old ear trouble, and some impairment of vision in the right eye, the result of a slight degree of atrophy following the severe optic neuritis.

Dr. G. A. SUTHERLAND.—*Case in which symptoms of intracranial tumour were relieved by trephining.*

R. C., male, aged 8. Admitted to hospital on April 21, 1906, with a history of headache, vomiting, and pain in the left ear. There was no clear evidence of there having been a discharge from the left ear. On admission, paralysis of both sixth nerves, the left being completely paralysed, and the right slightly affected, and double optic neuritis. Pulse 64-60 per minute, and respiration at times slow (12-14 per minute) and irregular. No evidence of ear disease. As vision was failing, on May 7 the skull was opened on the left side, and the temporo-sphenoidal lobe and cerebellum were explored. No evidence of intracranial pressure or local disease was discovered. He left the hospital on June 1 free from headache, and optic neuritis, and with only a slight trace of paresis of the left sixth nerve.

Dr. F. E. BATTEN.—(*a*) *Case of brachial plexus lesion.*

F. C., male, aged 18. Letterpress printer. Had influenza at Easter time, 1906. Fourteen days later had pain with sudden loss of power in the right shoulder and arm. No improvement took place, nor did the loss of power increase after the onset.

Motion.—There is wasting and marked loss of power in the right deltoid, the supra- and infra-spinatus and teres muscles. There is weakness of the triceps and trapezius, and to a lesser degree of the biceps. The supinator longus and muscles of forearm act well.

Sensation.—There is an area of complete anæsthesia and analgesia over the shoulder and upper portion of upper arm, and a wider area of relative impairment of sensation over the scapula and outer side of upper arm to the elbow.

Electrical reaction.—The deltoid, supra- and infra-spinatus, and teres, show complete loss of reaction to faradism, and sluggish response to galvanism. The pectoralis major and trapezius react more briskly to faradism than the corresponding muscles of the opposite side.

There is no weakness of the lower limbs. The knee-jerks are active, equal, and the plantar response is flexor.

(*b*) *Case of myopathy—exhibiting slow relaxation of muscles after muscular action.*

F. W., aged 37. Elder brother is said to have died of "locomotor ataxy" at 47.

For the last two years he has noticed weakness in the legs, and wasting of the thigh muscles.

The patient has weakness of the orbicularis palpebrarum and a myopathic facies. There is weakness and wasting of the muscles of both thighs, the right being more affected than the left. The left knee-jerk is greater than the right.

The electrical response of both anterior tibial muscles is diminished. The thigh muscles show similar changes.

When the patient grasps an object tightly it is some few seconds before he can fully relax his grip.

Dr. Rayner Batten.—*Congenital defect of left cervico-ocular sympathetic.*

Alfred B., aged 23. The pupils have always been unequal. The *right* pupil is active to light and accommodation. In a dull light it is much larger than the left, but is about equal to it in a bright light. The *left* pupil shows little if any reaction either to light or accommodation and remains nearly stationary. Both pupils dilate about equally under cocaine, but the right dilates more fully under homatropin and cocaine than the left.

Consensual reaction to light is good on the right side, not obtained on the left. No marked error of refraction.

V. R. = $\frac{6}{9}$ and Ji. at 12 inches.

V. L. = $\frac{6}{6} + \frac{6}{5}$ and Ji. at 12 inches.

Vision appears to vary.

There is slight ptosis of the left upper eyelid, but no recession of the eye-ball.

The patient sweats very readily on the right side of face and neck, but very little on the left side.

Dr. S. A. K. Wilson.—(1) *A case of spasmodic torticollis, with involvement of the abdominal muscles.*

W. H., aged 60, admitted to the National Hospital under Sir William Gowers on April 4, 1906.

The patient has always been delicate in health, and has always been very nervous and sensitive, suffering frequently from attacks of depression.

For five or six years he has had pain in the middle of the neck posteriorly, which he considered rheumatic. About two years ago, when run down with overwork, he found that his head was beginning to turn involuntarily to the left, and during the last six months the spasm has been practically constant. Latterly there has been depression of the head anteriorly, as well as rotation. Not long after the condition had appeared, he noticed that the abdominal muscles were taking part in the spasm, and that synchronously with them the head was moving in an antero-posterior direction.

In addition to occasional tonic rotation of the head to the left, coupled with depression of the chin on the chest, there is an almost constant fine nodding movement of the head in an antero-posterior direction, and it will be found that the recti abdominis are contracting more or less rhythmically though not equally. They are the seat of short abrupt irregular twitches which are insufficient to produce displacement either of the trunk or of the umbilicus. When patient takes a deep inspiration there is no spasm. As he rises to a sitting position the involuntary spasms give way to a firm voluntary contraction.

There is also sometimes irregular twitching of the erector spinæ on both sides. The movements disappear entirely in sleep.

(2) *A case of spasm of the diaphragm.*

W. L., aged 54, admitted to the National Hospital under Sir William Gowers on June 8, 1906.

Five years ago he had a severe attack of enteric fever when in India, and, while stil in bed, began to hiccough. He has hiccoughed ever since, the longest free interval being about twelve days. There is a curious periodicity in the attacks. For about the same time, he has complained of dyspepsia, of flatulence, and occasionally of water-brash.

The patient has an emphysematous chest, and a slightly dilated stomach. The involuntary movements are of the following nature: usually towards the close of the act of inspiration a sudden clonic contraction of the diaphragm occurs, and this descent of the diaphragm causes the abdomen to bulge. Just as the spasm takes place, the vocal cords may be seen by the laryngoscope to be spasmodically approximated, and thus air is prevented from entering the trachea quietly. The noise made, however, varies considerably. At the same time as the diaphragm contracts there is marked sucking in of the spaces above the

clavicles and above the suprasternal notch, apparently because the closure of the glottis has prevented the entry of air necessary to fill the vacuum made by the descent of the diaphragm. There is synchronous elevation of the soft palate. Alteration of respiratory rhythm voluntarily makes little difference in the condition. The movements do not disappear in sleep.

(3) *A case of sensory aphasia.*

J. T., age not known definitely, was admitted to the National Hospital, under Dr. Risien Russell, on July 9, 1906.

As far as is known he has always been healthy. He is right-handed, and it is believed has never been able to read or write well. A year ago his wife died, and this has preyed on his mind. Up to the time of his illness he was employed in the officers' mess of the third battalion of the Suffolks.

On April 6, 1906, when under the influence of alcohol, he fell from a cart and injured the left side of his head. He remained overnight in the military hospital, more or less unconscious, but left the next day apparently well. Two days later he returned in a half dazed condition, quite unable to express his thoughts. There has been no change since, except that his general health has improved.

At present he looks quite healthy, and does not complain of headache. There has been no sickness.

Vision normal. Optic discs normal. No hemianopia. Pupils slightly unequal, normal reactions. No facial asymmetry or weakness to speak of. Perhaps slight weakness of the right arm, compared with its fellow. Sensation unimpaired. No incoördination. Reflexes normal. Double flexor response. Abdominal equal.

Speech: articulation and phonation excellent. Little word deafness. Great word blindness. Cannot repeat a single syllable to order. Can sing tunes well, frequently with words. Can whistle accurately.

Cannot write. Cannot read. Can copy correctly written and printed language. Cannot read what he has copied. Can draw well. Cannot name any objects, but indicates their use perfectly. No apraxia or mind blindness.

Whenever he is engaged in conversation, he pours out a torrent of words and phrases, with frequent recurring utterance. His speech is nonsense, consisting chiefly of references to his children, as far as can be ascertained. It is accompanied, however, by remarkably rich and accurate gestures and pantomime.

Under the care of Dr. FERRIER. Shown by Dr. CARMALT JONES.—*Myopathy associated with antecedent anterior poliomyelitis.*

V. H., aged 7.

Complaint.—Loss of power of arms and legs.

Family history.—Nothing similar.

Previous history.—Aged 16 months; bronchitis. Frequent convulsions in teething. Walked at five years. Then lame on left leg. Four years ago, sores on left leg. Crutches for left leg. Quite strong in arms till winter, 1905, when weakness began in both arms and right leg. Progressive.

Present condition.—Mental; special senses; cranial nerves; sensation all unaffected.

Motor.—Very helpless. Muscles small, many wasted. Thorax mis-shapen; lateral curve to right. Marked wasting of pectoral girdle, especially left. Trapezius deltoid, pectorals, latissimus, supra-infraspinatus much wasted, especially left biceps, and brachialis anticus wasted, especially left. Pelvis tilted. Left ant. sup. spine raised. Slight lordosis. Left leg appears much shortened, wasted in calf. Right well shaped, thick and fibrous. Numerous old trophic lesions on leg. Hips—Right, all movements very weak; left, fair. Knees—Right flexion and extension very weak; left flexion fair. Ankles—Right flexion and extension fair; left held dorsiflexed tendon of ext. long. digitorum shortened. All movements very weak and limited; all toes much flexed.

Reflex.—Epigastric abdominal, brisk. Plantar. Flexor right. Absent left. Sphincters normal.

Electrical reactions.—None obtained in wasted muscles with any current that patient can bear.

Left leg, though most wasted, is the stronger of the two.

Under the care of Dr. ORMEROD. Shown by Dr. CARMALT JONES.—*Lesions probably hæmorrhagic in lumbar cord; with intracranial arterial degeneration.*

A. B., aged 42, carpenter.

Complaint.—Loss of power both legs; loss of sphincter control; headache, vomiting, loss of sight; gradual onset four years.

Family history.—Unimportant.

Previous history.—Good; venereal disease and risk denied.

Present illness.—Four years ago sudden numbness and loss of power, left leg; gradual recovery; able to work in eighteen months, though still lame. Two years ago headache and vomit-

ing ceased in six months; never well since. One year ago, pleurisy. Nine months ago loss of power both legs; headache, vomiting, loss of sight.

Present condition.—Emotional and dull; aware of this as a recent occurrence.

Special senses.—Smell, dull. Hearing bad; right (old middle ear disease), fair, left. Sight $\frac{6}{5}$ (with difficulty), right fingers only, left visual field, normal right. Disc—Right papillary retinitis, degenerated arteries, hæmorrhages: white spots at macula, simple advanced arterial disease. Left, pale, arteries bright and tortuous, early degeneration. Probably old amblyopia.

Cranial nerves.—Pupils normal, slight divergent strabismus when at rest, ocular movements free, other cranial nerves normal. Articulation slow and indistinct.

Sensation.—Headache chiefly occipital when present. Very slight relative anæsthesia and analgesia, left leg. Marked tenderness on pressure over lower dorsal and upper lumbar spines.

Motor.—Head and neck—upper extremities, movements normal. Thorax and abdomen move well with respiration. Trunk abdominal muscles act without deviation of umbilicus; but he cannot sit up without help. Erector spinæ acts well. Legs both weak in all movements, especially left, which is very weak.

Reflex.—Epigastric and abdominal absent. Plantar extensor (not invariable). Arm-jerks all very brisk. Knee-jerks, ankle-jerks, increased. Ankle clonus, R. and L. Sphincters, precipitate or delayed. Coördination, unaffected.

Viscera.—Normal. Vessels not sclerosed. Urine has contained trace of albumen, none at present. Appears to have had slight epileptic fits.

Under the care of Dr. ORMEROD. Shown by Dr. CARMALT JONES.—*Left hemiplegia, lesion in right crus cerebri, also muscular wasting, and unusual respiratory asymmetry.*

S. H., aged 36, married. Right-sided headache; left hemiplegia.

Family history.—Unimportant.

Previous history.—Always delicate.

Present illness.—September, 1905, confined; natural labour. October, 1905, right eye became painful and bloodshot; severe right-sided headache. April, 1906, diplopia; objects one above the other; transient. Became very nervous. Left leg grew weak, began to drag; left arm weak; could not do her hair.

Later, difficulty in swallowing; regurgitation of liquids; difficulty in breathing and swallowing.

Present condition.—Thin, ill-nourished.

Cranial nerves.—Pupils normal; ptosis right; deficient upward and lateral movements right eye; left ocular movements free. Weakness left face; upper and lower divisions less marked in emotional movement; jaw normal; palate moves better right than left; uvula deviates to right, marked in coughing. Phonation hoarse; deglutition difficult; tongue free.

Sensation.—Headache; giddiness; rotation of self and objects left to right. Partial left hemianæsthesia and analgesia, diminished position sense left fingers and toes.

Motor.—Right sternomastoid atrophic; and trapezius to less degree; left normal. Head goes over to left in backward movement. Thorax moves better right than left in forced and natural breathing. Abdomen moves very little; breathing chiefly thoracic. Limbs weak throughout, left definitely weaker in all movements.

Reflex.—Epigastric abdominal absent, plantar flexor right, extensor left. Sphincters normal. Deep all increased left. A.C. sustained left. A fine tremor is sometimes present in left arm. Slight ataxy left arm.

Pathological Specimens.

Dr. Leonard S. Dudgeon.—"*Bacillus of Hamilton Wright isolated from a case of Beri-Beri.*"

Dr. Gordon Holmes.—(1) *Two complete cases of amyotrophic lateral sclerosis.* (2) *Syringomyelia with a spinal glioma.* (3) *Friedreich's ataxia* (*from one of Dr. Pott's series of cases*).

Dr. J. Michell Clarke.—*Two specimens of cerebral tumour illustrating the production of hemiplegia of apoplectic onset by hæmorrhage into a tumour; in one of the cases without any previous symptoms.*

(1) From a man, aged 63, who was brought into the Bristol General Hospital apparently in an attack of ordinary apoplexy, but with the addition of well-marked optic neuritis. It was stated that he was in good health up to the onset of this attack.

The specimen shows a rounded tumour about two inches in diameter growing in the white matter subjacent to the ascending frontal and parietal convolutions. The growth is a glio-sarcoma, into which several hæmorrhages had occurred.

(2) From a woman, aged 44, who was admitted into Hospital in coma, which had come on suddenly eight hours previously. The left pupil was dilated. There were double optic neuritis, and hæmorrhages into the left retina. Death occurred twenty hours later. The temperature rose steadily to 106° F. at death. She had suffered from occasional vomiting after meals and slight headache for the previous three months, but the first sign of serious illness was stated to be the occurrence of convulsive attacks three or four days before admission.

The specimen is one of a large glioma in the left frontal lobe, into which hæmorrhage has taken place.

The specimens also illustrate a simplified method, devised by Mr. F. Leighton, of mounting brain-sections in glycerine jelly in glass cells.

Dr. C. E. Beevor.—*Specimens of brains injected simultaneously with five colours.*

Dr. Page May.—*Microscopical sections showing* (a) "*Degeneration of Monakow's bundle.*" (b) "*Degeneration of vestibulo-spinal tract.*" (c) "*Degeneration of pre-dorsal bundle.*"

THIS NUMBER OF "BRAIN" IS DEDICATED

AS A

TRIBUTE OF RESPECT AND AFFECTION

TO

JOHN HUGHLINGS JACKSON,

M.D., F.R.S.,

IN THE 50TH YEAR OF HIS MEDICAL PRACTICE

BY THE

NEUROLOGICAL SOCIETY OF THE UNITED KINGDOM.